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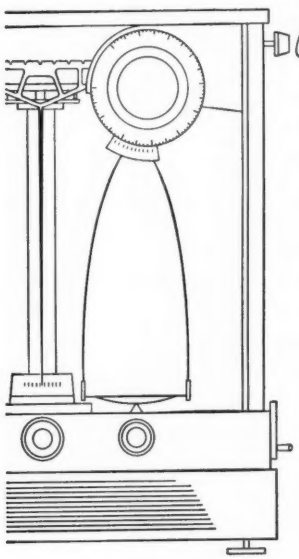

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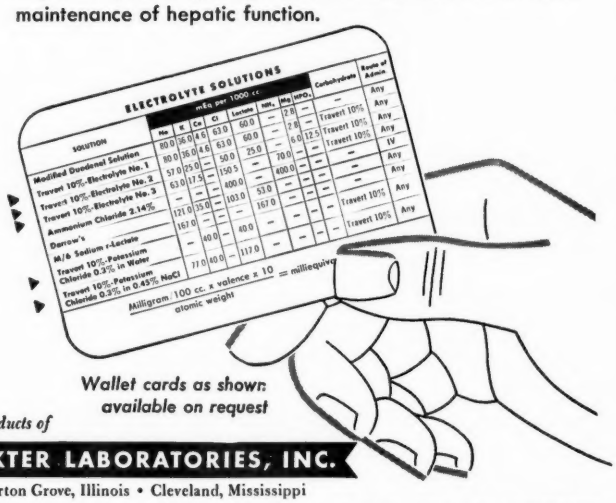

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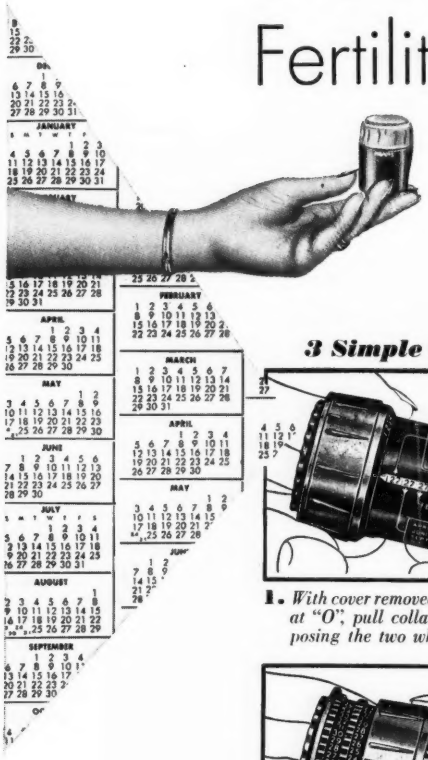

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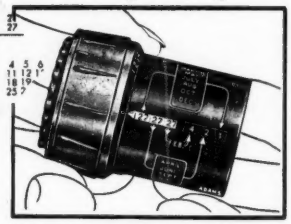
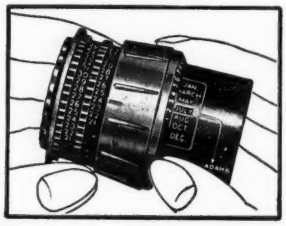
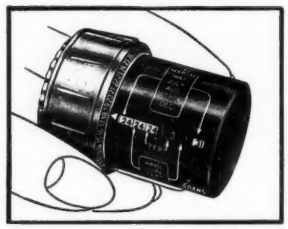


1. *With cover removed, set indicator at "O", pull collar to right, exposing the two wheels.*



2. *Shortest and longest cycles are set opposite each other—relock calculator by sliding collar back in place, with line over individual cycle variations.*



3. *Fertile period is read directly when indicator is set at date of menstrual onset.*

SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 97 AUGUST, 1953 NUMBER 2

THE LIMITATIONS OF RADICAL SURGERY IN THE TREATMENT OF CANCER

HARVEY B. STONE, M.D., F.A.C.S., Baltimore, Maryland

IT is repeating a truism to state that the past two decades have brought about a great extension of the limits of safety in operations. Better anesthesia, better control of infection, better knowledge of the physiology of respiration, of the heart and blood vessels, of body chemistry, of blood replacement, and of many other factors in the preoperative and postoperative care of patients have contributed to this enlargement of the possibilities of surgical intervention. As a consequence, many operations once regarded as maximum procedures have become commonplace and many never seriously considered before are being done with reasonable safety. It is quite natural that this enlarged freedom of surgical intervention should cause repercussions in the field of cancer treatment. Disease involving structures in the thorax, for instance, are now readily accessible to attack, which before offered little likelihood of success. Also procedures that had become standardized as a result of long experience, for the treatment of cancer in such anatomic regions as the breast, stomach, and pelvis, are being subjected to great modification. There has been extension of the area of resection, of the time involved in the performance of the operation, and, in general, of its magnitude and hazard. It would seem that the time has come for an assessment of this trend.

In undertaking an appraisal of what may be called the newer radicalism of cancer surgery, there are certain general qualifications that should be made at the beginning. It is important to limit our consideration to surgery designed for the treatment of cancer. The mere extensiveness or radicalness of a proposed operation is not so much under discussion as is the appropriateness of that sort of an operation for the therapy of cancer. For instance, surgical attack to correct a congenital fistula between the esophagus and the trachea in an infant may involve almost the same operative problems as the removal of a carcinoma of the esophagus—in fact the first problem may be technically more difficult than the second. Yet in most instances the first effort may be clearly necessary and the second quite obviously useless. The malignant disease may be so extensive that even the dubious reasoning that the patient is going to die anyhow would hardly be invoked. Thus an operative procedure of the newer radicalness may be precisely indicated in order to correct an anomaly, and the same type of operation may be distinctly contraindicated in many cases of a malignant lesion located in the same area. It would seem, therefore, that it is essential to restate and emphasize the reasons why surgery is used in the treatment of cancer.

To begin with, it may be stated that while x-ray, radium, and perhaps other agencies may be employed in special regions, with special forms of malignant disease. and for special purposes, surgery remains by all odds the best and

most successful method we yet have developed in the fight against cancer. It must also be stated, however, that it is far from a satisfactory method. Not only is the method costly in pain, disability, and money, but its results unfortunately leave much to be desired. One may say that the very basic principle of cancer surgery is crude and destructive. For, stated simply, that principle is to remove the growth with as much of the patient's surrounding tissues as is compatible with safety for life and for preservation of satisfactory health and function afterward. Obviously, this is not a precise and economical attack on the disease itself, but something perilously like burning down the barn to get rid of the rats. Yet, in spite of these drawbacks, it must be repeated that, at the present time, surgery remains the best means we have to deal with cancer.

Let us then accept that we shall continue to use surgery, but let us also try to define more specifically its purpose. At once it is seen that actually surgery may be employed for either one of two different purposes, and one should clearly distinguish between them. It may be employed with the consciously limited objective of palliation of symptoms, or for the larger aim of cure—which may better be called prolonged and indefinite recovery.

Many instances of palliative and very useful surgery will occur to every surgeon. The local removal of an advanced carcinoma of the breast may greatly alleviate the remainder of the patient's life. Anastomosis of the gallbladder or common duct to the alimentary tract, in cases of jaundice due to inoperable cancer of the head of the pancreas, is frequently a great relief. Resection of a growth in the colon, when liver metastases are present, may restore the patient to almost complete freedom from symptoms for a surprising length of time. In these and other similar situations a well standardized limited operation of minimal risk, brief duration, and short convalescence is the general practice. No one questions the usefulness of this type of surgery when wisely employed, and there should be no pressure to extend the scope of it because of the newer freedom of surgical adventures. To make a palliative procedure more radical is a contradiction in terms and in ideas.

It is in the second and major type of cancer surgery—that designed to accomplish a so-called cure—where the impact of surgical advance has really made itself felt and where any discussion of the newer radicalism in the attack on cancer really centers. Perhaps the first and most pertinent question that should be raised is this: Does the recently advocated extension of the field of ablation constitute a new principle or a new technique in the attack on cancer, or is it simply more of the same thing? The answer to this must be obvious. There is no change in the higher strategy of the war against cancer. It is simply that we have now better weapons to fight with, but the fight is along the same old lines. To repeat what was said earlier, it is still the principle of destroying as much tissue about the growth as can be done with due regard to safety of life and preservation of health and function. Here, of course, the point will properly be made that the newer surgery does just that—it does permit a wider removal with preservation of life in some cases. If this were all there is to be said on the subject, one would have no reason for further discussion. But the matter is not that simple. One must ask what is gained by the more extensive and destructive newer radicalism, and also what is lost by it? The problem thus becomes one of balancing.

The gain, in fact the only claim of gain, is to be looked for in an increase in the percentage of long term survivals. It may fairly be said that as yet an insufficient number of operations have been done over a long enough period of time to give a clear answer to this question. Further, it should be evident that the figures of long range survivals, when available, will need careful study. A small number of patients have been reported as living 5 years or more after one of the ultraradical operations. On the other hand, some clinics that undertook to apply certain of these operations to specific examples of cancer were led to abandon this practice because of disappointing experience. The largest group study with which I am acquainted, that of Brunschwig, reports a small number of survivors in about 100 ultraradical operations. This group was quite heterogeneous. The anatomic extent of the lesion and its pathologic character varied a great

deal. In fact, several of the cases included were not even malignant. The only common factor was the employment of the newer radicalism in the operations done. Obviously the fact that some survivors, even as small a percentage as in this report, may live for a number of years is a fact of considerable interest and perhaps of importance. It does not prove, however, that some of these same individuals might not have survived also for the same period of time following the usual classical cancer operations, or indeed if they had not been operated upon at all. Anyone familiar with the wide variation in the natural history of malignant disease knows this to be true. Anyone who has done a limited operation and knowingly left behind distant metastases may have had the surprising experience to find the patient living after 4 or 5 years. Unfortunately also, anyone who has had much and long experience in the field of cancer surgery has had the dismaying experience of encountering recurrence 10, 15, or even 20 years after an apparently successful operation. These facts are recalled, not to discredit serious and heroic efforts to improve our results in cancer therapy; it is simply to amplify the statement made above that much more experience must accumulate and must be critically analyzed before we have evidence of loss or gain in the long term survival rate from cancer because of the ultraradical types of operation. If the writer may hazard a guess as to what the future will show, it would be that there will be some improvement in our long range survivals, but that it will be in the nature of a minimal percentage—perhaps 3 or 4 cases per hundred.

It becomes necessary now to attempt an estimate of the disadvantages of the newer method. One thinks first, naturally, of the greater immediate mortality. Indeed this was formidably high in the beginning of the development of the newer radicalism, which is only to be expected in the developmental stage of any extensive surgical procedure. The history of the development of our currently commonplace operations often shows a similar story. As the newer methods have become more practiced and perfected, the mortality has materially diminished. It still remains notably higher than in the classical type of operations, however, and probably always will remain so. Indeed it is likely that this increase in immediate mortality will more than offset the expected increase in 5 year survivals. In considering the question of mortality one must not overlook a tendency to confusion resulting from certain commonly used terms. One thinks of "immediate mortality" as operating room or recovery room death. It should be appreciated that deaths occurring in the early postoperative period—sometimes called hospital deaths to distinguish them from operating room deaths—really all fall into the group of deaths immediately following the surgical procedure. In this group, in spite of improvement in the direct operating room mortality, there still remains a very considerable increase in the losses as compared with classical cancer surgery. The inclusion of all the cases of death in the interval closely following the operation amounts to a serious disadvantage of the newer cancer surgery.

But increased loss of life is by no means the only loss that is increased following the ultraradical methods. In the large majority of patients recovering from the classical operations for cancer there is a return to good general health and function for much of the period of life left to them, whether that period be relatively brief or indefinitely prolonged. This cannot be said for the postoperative experience of many who have survived the ultraradical procedures. In all too many cases the resulting damage in the form of mutilation, loss of normal functioning, distress and discomfort, and failure to regain weight, strength, and normal blood count is unquestionably far greater than after the usual radical operations. Not only are these unfortunate sequelae more intense; they last much longer. Often indeed they continue until ended by the patient's death. The exact nature of these postoperative misfortunes will depend, of course, on the particular structures that were sacrificed or extensively damaged in the operation. Thus in the head, neck, and extremities, loss of speech or swallowing, inability to walk or to work, or shocking disfigurement may result. In the alimentary tract, inability to eat, to retain, to digest, or to absorb food may resist all

efforts at correction, although in a number of instances postoperative regimen and careful management after many months may bring about a very considerable improvement. In pelvic operations the subsequent disposal of the excreta of kidneys and bowel may render life anything but agreeable. That these statements are true is borne out, not only by common knowledge, but by the appearance in the literature of articles devoted to efforts to correct or improve the lot of survivors of ultraradical cancer surgery. Many of these are interesting and ingenious plastic operations to construct a substitute arrangement for the organs that have been destroyed. One such procedure recently reported by Wenger described a many stage reconstructive program at each step of which biopsy study was made for any evidence of persistence of the original malignant disease. None was found. After the final completion of the long surgical reconstruction, a fairly satisfactory functional result was obtained. The unfortunate sardonic postscript to this ingenious and protracted effort was the statement that a few months after completion of the last step the patient died of metastases of the original disease.

A factor that is not exactly medical but that is eminently practical is the much increased cost in money, direct and indirect, that so often follows these newer ultraradical operations. In a day when all costs, including especially hospital and nursing costs, are so heavy, and when loss of earning power means so much to many families, the difference between a 1 month and a 6 months' period of disability is something that cannot be lightly dismissed as of no importance. Nor will it do to say that this temporary financial disadvantage is offset by the longer life and increased chance of protracted recovery or cure following the ultraradical surgery. If one were to charge against the greater cost to all the patients, in an average group of 100 ultraradical operations, the greater earning power of the few who survived, say 5 years, there seems little doubt at present that the net expense to the group would be considerably greater than if the usual classical operations had been done on these patients.

This last comment brings us back to the statement made earlier, that we are confronted with a problem in balancing the loss and gain involved in the newer radicalism before we can evaluate it or try to set its limitations. And this is no easy task. So much hinges on the question of how considerable is the increase in the long range survival, and, as has been said, our data just now are quite inadequate to answer this basic question. It will not do, I think, to attempt to evade this issue by saying that even if there is only one chance in a hundred of prolonged recovery, we are not justified in refusing it to any individual who presents the concrete problem of whether or not to undertake an ultraradical operation. We must weigh against this long chance the things that can and do happen in the other 99 cases. We must ask these other questions, and give these answers. What is the probability that we shall shorten the patient's actual time of survival? It is great. What is the likelihood that the survival period, long or short, will be one of distress and disability? It is great. What is the chance that the patient will be committed to more costly treatment? It is great. Finally what is the chance that the patient will die ultimately of his disease, despite the heroic surgery? It is very great.

The discussion so far has concerned itself with generalities. It has been the writer's effort to portray his own thinking on the question of the value to surgery and to the victims of malignant disease of the newer wide extensions of the field of ablative operations. It will be evident that the writer is a skeptic as concerns the desirability of this type of operation coming into general use. Quite frankly, I think this would be unfortunate.

Is it to be concluded, then, that there is no increment of value in this movement? I think this is certainly not true. Can one, then, set up some approximate guiding principles for the avoidance of ill-judged attempts at ultraradical surgery? Can this be done without losing any valuable additions to our surgical resources that the newer radicalism may offer? Certainly it is worth while to make the effort.

All should agree that something more than the customary facilities for the usual surgical undertakings is necessary. There must be a staff of operating room and laboratory personnel trained and ready to meet such emergency

situations as sudden large losses of blood, obstruction of the airways, or cardiac arrest. The surgeon himself should possess outstanding technical skill and courage. Most of all he should have added to these qualities wide general experience and sound common sense, the qualities that form good judgment. It has been said that exceptional skill and daring, when not controlled by good judgment, make a dangerous combination. All these necessary technical and personnel requirements constitute limitations to the employment of ultraradical surgery of any sort.

The nature of the cancer itself may make the employment of ultraradical operations unwise. Most malignant lymphomas are not best treated by extensive surgery. These forms of malignant tumors are essentially not diseases of particular anatomic organs, but rather of a specific type of tissue that is widespread throughout the body. Hence the most extensive possible local excision still cannot be regarded as basically sound. Lymphosarcoma and Hodgkin's disease primary in the stomach, for instance, should be handled by simple palliative operations, biopsy, and either radiation therapy or one of the recent chemical remedies that are of value in these diseases. Forms of malignant disease that tend to spread chiefly or largely by blood stream dissemination are not suited to ultraradical surgery. It seems ill advised to subject a patient to a hemipelvectomy for a malignant melanoma of the foot. Such an operation is quite ineffective against any extension of the disease which may have already occurred by way of the blood stream. So far as lymphatic spread is concerned, nearly the same degree of effective removal can be accomplished by extensive dissection of the channels in the leg and the nodes in the groin and iliac regions, without the crippling disability and mutilation of a hemipelvectomy. Note that such objections do not apply to hemipelvectomy for such conditions as osteosarcoma of the ischium or pubis.

The extent of the cancer discovered at operation may be a positive contraindication to any form of radical surgery, to say nothing of ultraradicalism. The writer has little patience with those who would treat a cancer of the stomach by total gastrectomy combined with removal of the spleen, the left lobe of the liver, the major portion of the pancreas and the transverse colon, in a case in which there is already widespread nodular dissemination over the omentum and the peritoneum generally. Yet such operations have been done. Even without the nodular dissemination, if the obvious disease has extended to numerous adjacent organs, their removal along with the primary lesion can offer only a very remote chance that the growing microscopic periphery of invasion has been extirpated. Similarly when carcinoma of the rectum has extensively invaded the bladder base, the lateral pelvic structures and the aortic nodes for a long distance, a total pelvic exenteration seems to me indefensible. The chances of ultimate cure in such cases as these are minimal and the operative risk, the protracted postoperative care, and the permanent disability are maximal. If this paper has no other effect than to discourage these manifestations of ultraradicalism, it will have served a useful purpose.

Does this mean that there is no place for efforts to apply the enlarged safety of surgical operating to the treatment of malignant disease? Certainly not. There is a movement to utilize total gastrectomy as a routine method of treatment for cancer of the stomach. Arguments of some merit are advanced in support of this idea. Although persuasive, these arguments are not convincing to the writer but at least the plan deserves a thorough trial. There are, no doubt, other situations where extensions of our present operative methods might be a step forward. To frown on all efforts to utilize our enlarged surgical liberty in the treatment of cancer would be blind conservatism, and a block to progress. But it is equally blind radicalism to reason that because it is now *possible* to do certain extensive operations with a new degree of safety, it therefore is *sensible* or *desirable* to do them. It is still true that the surgeon's greatest quality is his judgment and sound common sense, and his first duty is to his individual patient. Also, in assessing any method of treating a disease, careful consideration of the pathologic processes involved is a basic necessity.

Furthermore, when the *gross* extent of malignant disease is such that heroic anatomic

destruction is required to remove it, the expectation that these measures will eradicate the invisible *microscopic* spread of the malady requires an even more heroic optimism.

Finally let us not forget the old admonition that the doctor, in his efforts to do good, should above all be careful not to do harm.

Aside from and above the strictly scientific aspects of any problem in clinical medicine there are its humanistic relations. To quote Walshe in his Thayer Lecture on the "Nature of Clinical Medicine": ". . . in the application of science to the practice of medicine we need prudence, for the doctor's action must have regard to the whole good of the patient." In the situation under discussion, the exercise of this humanistic prudence would require, among other things, that the patient be fairly and fully informed of the possible benefits and dangers that proposed ultraradical surgery involves. By fairly and fully, is meant without either the zeal of salesmanship or the gloom of pessimism. If such a presentation is properly made and the patient elects to undergo ultraradical surgery, knowing its limitations, the surgeon will not only have done his full duty, but should be able to approach his task with a lighter heart and a freer mind.

Perhaps enough has been said to disclose the writer's views on the purely medical aspects of the subject of this paper. I wish to enlarge the discussion to include certain comments on both personal and philosophic matters. It is no secret that in informal arguments about ultraradical cancer surgery, the defenders of opposing views sometimes resort to adverse judgments on the qualities of their opponents. Thus the advocates of the newer radicalism charge that those who disapprove of it are lacking in courage, have not the physical stamina to sustain the long ordeals of such operations, nor the elasticity of mind to welcome innovations. The other group, in turn, say that the radicals seek personal prestige and practice at the expense of the patient's best interests, that they are handicraftsmen not physicians, and that showmanship rather than judgment guides them. Now while one may admit that there is a trace of truth in both sets of charges, the great truth that lies behind these *ad hominem* arguments is that two great conflicting currents are present in every field of human activity. In painting, sculpture, music, and literature, the advance guard confronts the traditionalist. In religion there is division between the fundamentalist and the modernist. In politics the conservative and the radical dispute for men's minds. Nor is this a new and recent state of affairs. At every moment of human history, mankind has been divided between those who desire to improve and correct what they consider the evils of their day and those who seek to preserve from destruction what they hold valuable in the *status quo*.

A new political and social philosophy led to the triumphs and also to the horrors and excesses of the French Revolution. On the other hand the whole basis of civilization rests on the fact that man is essentially a conservative animal. He can transmit and preserve from generation to generation the fruits of experience, the appreciation of the virtues learned by his forebears, the preservation of standards of conduct, social relations and beliefs embodied in laws, customs, and traditions. The whole development of science depends on the continuance of learning, building new increment on the firm foundations already built.

In short, we must see human progress equally dependent on the sturdy retention of the proved good, and the adventurous search for the unknown better. The automobile without brakes is a dangerous agent of destruction. The automobile without an engine is simply a pile of metallic junk.

The philosophy of this situation was well known to the Greeks as the golden mean. It has a direct bearing on the problem of our subject in this paper and indeed offers its solution.

We must study carefully the limitations, as well as the possibilities, of the new ultraradicalism in the surgery of malignant disease before its proper place and useful employment can be determined.

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PRIMARY TUMORS OF THE DUODENUM

RAY E. EBERT, M.D., GERALD F. PARKHURST, M.D., OAKLEY A. MELENDY, M.D., and MELVIN P. OSBORNE, M.D., F.A.C.S., Brookline, Massachusetts

RECENT experience with successful surgical resection of two primary carcinomas of the third portion of the duodenum stimulated a review and report of the cases of primary tumors of the duodenum seen at Boston City Hospital.

These tumors are rare but important because of increasing accuracy in diagnosis and successful surgical resection. Numerous articles have summarized scattered reports of duodenal malignant tumors, but only a few contain statistics on benign lesions. Benign lesions only occasionally give rise to clinical manifestations and are usually incidental findings at autopsy. Malignant lesions frequently metastasize before becoming symptomatic and, until recently, surgical resection had not been attempted or successful because extension had occurred by the time the diagnosis was made.

INCIDENCE

Raiford reported that benign tumors were found in the small intestine in 0.16 per cent of 56,500 autopsies. Most of these appeared in the duodenum and ileum. Among benign tumors of the duodenum collected in 1945 by Hoffman and Grayzel (2) there were 21 adenomas, 11 myomas, 8 pancreatic rests, 7 adenomas of Brunner's glands, 5 hemangiomas, 4 lipomas, 2 fibromas, 2 cystic tumors, 2 lymphangiomas, 1 fibroadenoma, 1 argentaffinoma, 1 gastric rest, and 1 fibromyoma.

Malignant tumors of the duodenum, according to Ewing, constitute 2 to 3 per cent of all the neoplasms of the gastrointestinal tract. Of the 228 cases of cancer of the small intestine collected by Hoffman and Pack (3), 45 per cent occurred in the duodenum and 55 per cent in the jejunum and ileum. The commonest location was the second portion of the duodenum and the next commonest the lower end of the ileum. Based on the occurrence in 487,695 collected autopsies, Kleinerman, in 1950, found the incidence of primary cancer of the duodenum to be 0.035 per cent.

Most malignant tumors of the duodenum are carcinomas and based on their anatomic site have been classified as supra-ampullary, periampullary and infra-ampullary. Of the 455 accepted cases of primary carcinoma of the duodenum in the literature up to 1948, 102 or 22.5 per cent were supra-ampullary, 268 or 59.2 per cent were periampullary and 83 or 18.3 per cent were infra-ampullary. Several authors agree that periampullary lesions occur more commonly, but this is an extremely difficult point to assess because carcinoma arising in the head of the pancreas, the ampulla of Vater, or in the bile ducts may be difficult or impossible to differentiate from carcinoma arising in the periampullary duodenal mucosa. Both benign and malignant tumors of the duodenum tend to occur in the middle and older age groups. Malignant tumors have been reported in the age range of 26 to 90 years with an average of 52 to 55 years. Males predominate with a ratio of about 3:1.

The etiology of both benign and malignant duodenal tumors is unknown. The majority of the carcinomas appear to arise in duodenal mucosa. An occasional one may arise from malignant degeneration of an ulcer as suggested by Jefferson. Anaplastic changes in Brunner's glands and polyps are possible sources, but again are not often seen. Twenty-three and one-half per cent of heterotopic pancreatic rests arise in the wall of the duodenum. Such factors as the irritative properties of bile, pancreatic and gastric juices, and the anatomic fixation of the duodenum have been considered predisposing but not causative elements.

MATERIAL FOR STUDY

Twenty-three primary tumors of the duodenum have been seen at the Boston City Hospi-

From the Fifth Surgical Service and the Mallory Institute of Pathology, Boston City Hospital, Boston, Mass.

TABLE I.—BENIGN TUMORS OF THE DUODENUM

Case No. Age, years Sex	Site of tumor	Gross description	Microscopic diagnosis	Other features
1 64 F	Duodenum	Two nodules of yellow tissue, 0.6 cm. diameter	Argentaffinoma	Incidental finding
2 63 M	First portion duodenum	White nodule, 1 x 1 cm. diameter	Argentaffinoma	Incidental finding
3 60 F	First portion duodenum	White nodule, 0.3 cm. diameter	Argentaffinoma	Incidental finding
4 72 M	Second portion duodenum	Polypoid mass 3 x 2.5 cm.	Neurofibroma	Jaundice due to obstruction of ducts (see text)
5 54 F	First portion duodenum	White nodule, 0.8 cm. diameter	Leiomyoma	Incidental finding
6 69 F	Duodenum	Two nodules, each 0.3 cm diameter	1 Leiomyoma 1 Neurofibroma	Von Recklinghausen's disease; hemangioma of ileum; meningioma
7 65 M	Second portion duodenum	Pedunculated mass 1.3 cm. length	Lipoma	G.I. hemorrhage of undetermined origin; cerebral hemorrhage
8 75 F	Third portion duodenum	Submucosal nodule, 0.5 cm. diameter	Lipoma	Incidental finding

tal in the past 50 years. Eight of these were benign and 15 were malignant. Three carcinomas were surgically resected, 2 of which are herein reported. Twenty of the lesions were found in 25,000 autopsies at the Mallory Institute of Pathology.

PATHOLOGIC SUMMARY

Benign tumors (Table I). Eight cases are presented, representing an incidence of 0.032 per cent. Three occurred in males and 5 in females with ages ranging from 54 to 75 years. Three of the lesions were argentaffinomas, 2 of which were in the first portion of the duodenum; the location of the third was not given—2 of these have been reported previously (7). Two were neurofibromas, one in the second portion of the duodenum, the other not given. Two were lipomas, one in the second portion and one in the third. One patient had both a leiomyoma and a neurofibroma. Pancreatic and gastric rests are not included in this series.

In 7 of these patients the tumors were incidental findings. One patient (Case 4) had a polypoid neurofibroma which measured 3 by 2.5 centimeters and which was located just above the separate entrances of the common bile and pancreatic ducts which were 2 millimeters apart. Structurally this tumor did not encroach upon the ducts, but during life it probably compressed their ostia with intermittent obstruction. The patient had been jaundiced. At autopsy there was fat necrosis of the pancreas, acute cholecystitis with empyema of the gallbladder, acute cholangitis, and pericholangitis. Another patient (Case 7) had a pedunculated lipoma in the second portion of the duodenum with massive gastrointestinal hemorrhage and cerebral hemorrhage. At autopsy no bleeding point could be found in the gastrointestinal tract and no mucosal ulceration could be seen over the tumor.

Malignant tumors (Table II). Fifteen cases are presented. Twelve of these are autopsied cases and represent an incidence of 0.048 per cent. Six of these tumors have been previously reported by Nickerson and Williams. Three were surgically resected; 2 will be discussed further. The third patient underwent radical pancreatoduodenectomy in 1938 but died 2 weeks after operation.

Of the 15 tumors, 3 were sarcomas and 12 were carcinomas. Seven were in males and 8 in females with ages ranging from 30 to 78 years. Five of the lesions were supra-ampul-

TABLE II.—MALIGNANT TUMORS OF THE DUODENUM

Case No. Age, years Sex	Site of tumor	Gross description	Microscopic diagnosis	Metastases	Other features
1 37 F	Supra-ampullary	Annular mass 2.5 cm. from pylorus 5x3x3 cm.	Adenocarcinoma	Liver	Vomiting 8 mos.; hypochromic anemia
2 61 F	Supra-ampullary	Ulcerated 3.3 cm.	Adenocarcinoma	Falciform ligament, retroperitoneal and mesenteric nodes	Vomiting 1 yr.; epigastric pain and jaundice; stone in common duct
3 30 M	Infra-ampullary	Villous mass 3x3 cm.	Adenocarcinoma	Liver, peritoneum, periaortic nodes	Dyspnea, weakness, pain—2 mos.; gastroenterostomy for perforated gastric ulcer 4 yrs. previously
4 50 F	Periampullary	Fungoid mass 5.4 cm.	Adenocarcinoma	Peripancreatic. gastrohepatic and periaortic nodes	50 lb. weight loss in 1 year; vomiting
5 72 M	Supra-ampullary	2 cm. ulcer	Adenocarcinoma	Liver, lung, periaortic nodes, compression of common duct	Abdominal pain; vomiting, jaundice 3 weeks' duration; also ca. of prostate
6 60 M	Supra-ampullary	Annular infiltrative tumor, size not given	Adenocarcinoma	Peripancreatic and periductal lymph nodes, lungs, liver, adrenals, bone marrow	15 lb. weight loss 3 wks., weakness, dyspnea, jaundice
7 62 M	Supra-ampullary	Ulcerated 2x1 cm.	Adenocarcinoma	Carcinomatosis peritonei	Perforated with peritonitis
8 78 F	Periampullary	Polypoid mass 5 cm.	Adenocarcinoma, common duct not involved	None	G.I. bleeding; congestive failure
9 63 M	Supra- and periampullary	6x8 cm. annular mass 2 cm. from pylorus	Adenocarcinoma	Invasion of common duct	Wt. loss, dyspnea, ankle edema; congestive failure
10 53 F	Infra-ampullary	Annular constricting 3 cm.	Adenocarcinoma	None	Surgical resection
11 71 F	Infra-ampullary	Ulcerated annular mass 6 cm. length	Adenocarcinoma	Lymphatics and 1 out of 7 regional lymph nodes	Surgical resection
12 49 F	Infra-ampullary	Ulcerated 7 cm. mass	Adenocarcinoma	None	Surgical resection; hepatic metastases at autopsy
13 70 F	Periampullary	Polypoid mass	Leiomyosarcoma	None	Abdominal pain, weakness
14 70 M	Periampullary	Fungating mass 3 cm.	Leiomyosarcoma or fibrosarcoma	Peritoneum, pleura, liver, retroperitioneal fat	Abdominal pain, nausea, vomiting, obstipation. Ca. of rt. kidney with no metastases
15 65 M	Infra-ampullary	Ulcerating tumor 3X3 cm.	Leiomyosarcoma	None	Wt. loss, abdominal pain, diarrhea 2 mos. duration

lary, 4 periampullary, and 5 infra-ampullary. Two sarcomas were periampullary and 1 infra-ampullary. Five of the lesions were ulcerated, 1 having perforated with generalized peritonitis. Five were annular and 2 were polypoid tumors. Two were described as fungating masses and 1 was villous. Extension or metastasis was present in 10 (66 per cent) of the cases. Lymph node involvement was described in 6, metastasis to the liver in 6, peritoneum in 3, lungs in 2, and 1 each to the adrenals, bone marrow, pleura, falciform ligament, and common bile duct.

During the period of time covered by this study, there were 14 ampullary carcinomas described. It is impossible to determine whether these tumors originated in ductal or duodenal mucosa. From a surgical or physiologic point of view it makes little difference.

SURGICAL ASPECTS

Benign tumors. Benign tumors of the duodenum when diagnosed can usually be treated by local excision. Generally their presence will be manifested by hemorrhage or obstruction, and they can be demonstrated by x-ray

studies or visualized at duodenotomy. If the common bile or pancreatic ducts are obstructed, a transplantation of the ducts or a shunt procedure may also be necessary.

Malignant tumors. Resection of malignant lesions of the duodenum is often not feasible because the majority of patients (66 per cent) have metastasis at the time of diagnosis. Palliative procedures such as gastroenterostomy, duodenojejunostomy, and biliary decompression have been reported with an average survival time of 21 months. In those patients with localized lesions we believe that attempted cure, radical resection of the duodenum and pancreas when necessary, or segmental duodenectomy as reported herein should be considered. Reported survivals range from 3 months to 3 years. Most localized infra-ampullary carcinomas of the duodenum have been treated by segmental resection and end-to-end anastomosis of the duodenum and the upper jejunum. Among about 70 proved cases of primary infra-ampullary duodenal carcinomas reported by 1950, Shallow, Wagner, and Manges found that 13 of the 15 resected cases had some type of segmental resection with survivals of 3 to 6 years. Experience to date suggests that segmental resection rather than radical pancreatoduodenectomy is the treatment of choice, since a comparable survival time seems to be obtained with lower mortality and morbidity. Duodenal carcinoma seems to resemble that of the left colon in terms of rate of growth, percentage involvement of liver and distant metastatic sites, and survival time after palliative operations. It is not associated with the characteristic early, wide metastases and short survival time of carcinoma in the stomach or pancreas.

Two primary infra-ampullary carcinomas of the duodenum have been segmentally resected on the Fifth Surgical Service at the Boston City Hospital.

REPORT OF CASES

CASE 1. H.K., a 71 year old widowed white female, was admitted to the Fourth Medical Service in February 1950 because of progressive weakness and epigastric pain. Present illness consisted of 1 year of increasing migrating upper abdominal and periumbilical cramping and burning pain with some knife-like radiation pain to the left chest and back. Symptoms came in attacks lasting about 30 minutes and were associated with weakness and profuse perspiration, and occasionally nausea and vomiting, sometimes coffee-ground and with occasional black and tarry stools. There was a 5 pound weight loss. Past and family history were not contributory. Examination demonstrated a normally developed, obese, pale female with marked upper abdominal tenderness. Laboratory studies were normal except for a hematocrit of 26 per cent with correspondingly low hemoglobin. The stools were guaiac and benzidine negative, and gastric analysis showed free hydrochloric acid without histamine stimulation. X-ray examination demonstrated a rigid area of narrowing 14 centimeters beyond the pylorus, interpreted as indicating carcinoma of the third portion of the duodenum. Roentgenograms for metastasis were negative.

Operation was planned but delayed because of a superficial migrating thrombophlebitis involving both legs which was treated with elastic bandages. On the fifteenth hospital day, after 2 blood transfusions, exploratory laparotomy disclosed a 2 centimeter firm, circumferential, localized lesion of the third portion of the duodenum lying behind the superior mesenteric vessels. This was resected along with duodenum up to a point 1 centimeter from the ampulla of Vater with 26 centimeters of the upper jejunum and attached mesentery. End-to-end anastomosis of the jejunum, which had been passed behind the superior mesenteric vessels, was accomplished over clamps with a single row of interrupted Halsted mattress sutures of fine silk. Pathologic study of the specimen reported a duodenal adenocarcinoma with involvement of 1 of 7 lymph nodes examined. The patient's postoperative course was uneventful. She was maintained on gastric suction for 4 days and then started eating a convalescent ulcer type of diet. A 6 day course of intramuscular heparinization was undertaken on the second postoperative day because of recrudescence of thrombophlebitis. The thrombophlebitis cleared and the patient was discharged on her fourteenth postoperative day. Twenty-five months after operation the patient continued to be in good health with no suggestion or recurrence of the malignant disease. However, recently she was readmitted to the Boston City Hospital with jaundice and was found to have local recurrence of the duodenal tumor at operation. A palliative cholecystoenterostomy and gastroenterostomy were done.

CASE 2. R.M., a 53 year old white housewife, was admitted to the Fifth Surgical Service of the Boston City Hospital on January of 1951 because of abdominal bloating after eating, increasingly persistent, dull, cramp, nonradiating epigastric pain, and vomiting of 3 months' duration. Symptoms usually occurred after eating and were relieved by vomiting. No blood had been noticed and no tarry stools. There was a 15 pound weight loss and increasing fatigability and weakness. Past history and family history were not remarkable.

Examination demonstrated a normally developed, moderately obese female who was in no distress. The abdomen was negative to examination except for lower abdominal scar (cesarean section 27 years before) with a small hernia through it. Laboratory examinations were not remarkable except for stool guaiac test 3+. Hematocrit was 39 per cent. X-ray studies demonstrated nonopaque calculi in the gallbladder, diverticulosis of the sigmoid colon and a partly obstructing right lesion in the third portion of the duodenum, interpreted as carcinoma. On the eighth hospital day, after gastric decompression, exploratory operation was undertaken through a transverse upper abdominal incision. There was a 3 centimeters long, napkin-ring like, circumferential lesion which partially obstructed the third portion of the duodenum behind the superior mesenteric vessels without any fixation to adjacent structures. No evidence of metastasis could be identified. Therefore, the duodenum was resected from a point just below the ampulla of Vater down to include 20 centimeters of the upper jejunum with its attached mesentery. The upper jejunal stump was passed behind the superior mesenteric vessels and an end-to-end anastomosis was made by using a seromuscular layer of interrupted horizontal mattress sutures of fine silk over an inner continuous fine catgut suture through the bowel wall. The patient's postoperative course was fairly uneventful with moderate obstructive difficulties for about 10 days, but after that the ability to take a progressive ulcer type of diet.

The patient remained in good health for 1 year but was readmitted to the Fifth Surgical Service in January of 1952 because of upper abdominal pain, weight loss, weakness, and vomiting. Exploratory laparotomy was undertaken to determine any possible palliative surgery or possibly to perform cholecystectomy if symptoms were best explained by the known gallbladder disease. The patient was found to have a large tumor mass growing in the root of the mesentery near the primary branches of the superior mesenteric vessels and to have a primary carcinoma of the right colon. The area of the old duodenal anastomosis was intact and there was no gastric dilatation or evidence of obstruction. No metastases were observed in the liver. It was believed that this patient had a carcinoma of the right colon with advanced mesenteric metastases as the explanation for her difficulty. Biopsy studies comparing a biopsy of the metastatic tumor mass with sections taken from the tumor in the right colon and the original duodenal tumor showed an adenocarcinoma, the histologic structure of which resembled the colonic tumor more than the original duodenal tumor. A palliative terminal ileectomy and right colectomy with end-to-end transverse colostomy were performed. This patient died in May of 1953 and was found to have had recurrence of duodenal tumor rather than metastatic disease from the carcinoma of the right colon at autopsy.

Thus, it seems clear that in these 2 cases, at least, cure might only have been sought by a more radical pancreatoduodenectomy.

SUMMARY

Twenty-three primary tumors of the duodenum, 8 benign and 15 malignant, are presented. Twenty of these tumors, 8 benign and 12 malignant, represent an incidence of 0.08 per cent in 25,000 autopsies. There were 3 argentaffinomas, 2 neurofibromas, 2 leiomyomas, 2 lipomas, 12 carcinomas, and 3 sarcomas. Sixty-six per cent of the malignant tumors showed metastasis.

Three adenocarcinomas were surgically resected. Two of these were infra-ampullary localized lesions and had segmental resection of the duodenum with survival. Both cases, presented in detail, had end-to-end anastomosis beneath the superior mesenteric vessels. One patient is alive and well 12 months after operation. Twenty-five months after resection the other patient had a new carcinoma of the cecum with inoperable metastases.

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RELIEF OF POSTTHORACOTOMY PAIN

W. RALPH DEATON, JR., M.D., Greensboro, North Carolina, and
H. H. BRADSHAW, M.D., F.A.C.S., Winston Salem, North Carolina

THE control of pain following thoracic surgery is a problem of considerable magnitude. It is imperative that the patient breathe deeply and cough frequently to keep the lungs fully aerated and to prevent bronchial secretions, purulent material, and at times blood, from accumulating and causing atelectasis. If analgesics are withheld or given only in small amounts, pain tends to inhibit deep breathing and coughing. Analgesics in a sufficient amount to control the pain fully usually diminish the cough reflex and respiratory excursion, to permit the same result as occurs if analgesics are withheld, namely, atelectasis. Thus, a compromise is usually attempted, with the hope that sufficient analgesic can be given to control the pain, without depression of respiratory volume or coughing. This balance is difficult to achieve. In the surgical treatment of pulmonary tuberculosis the problem becomes even more important than in other thoracic surgery, as the danger of dissemination of the disease through retained sputum is always present.

The value of intercostal nerve block in relieving pain of thoracic origin is common knowledge. However, with the usual local anesthetic (procaine), the duration of anesthesia is only a matter of a few hours, and the repeated injections necessary for prolonged anesthesia shortly become obnoxious to both the patient and the doctor. Blades and Ford introduced a method of producing continuous intercostal blocks through the use of minute plastic catheters threaded down to the pertinent intercostal nerves, and through which procaine is administered every 3 hours. The catheters are inserted at the completion of the operative procedure and are brought out of the wound in a novel manner that facilitates the repeated administration of procaine. This is indeed an improvement over repeated percutaneous injections of procaine but demands a fair amount of attention, and can be used only to relieve postoperative pain.

Several reports on the satisfactory performance of a new long-lasting local anesthetic solution, efocaine, for the relief of postoperative pain following various surgical procedures prompted a trial of it to induce intercostal nerve block for relief of pain following various thoracic operations. In view of the variability of the pain threshold from one patient to another, as shown beautifully by Papper in a study of postoperative pain, it was decided to use patients requiring multiple operative procedures as controls. Even numbered patients with planned multiple procedures, such as routine thoracoplasty or tailored thoracoplasty following resection, received an efocaine block at the second operation, while odd numbered patients were blocked at the first and third operations (a third operation was performed in 6 cases). Thus, patients served as controls for themselves, a particularly satisfactory method of control, in view of this variability of the pain threshold. Neither the patients nor the ward nurses knew which patients received efocaine; the postoperative orders were precisely the same in either case.

As an objective method of evaluating the effect of efocaine, the doses of analgesics given on the day of operation and the first 3 postoperative days were tabulated. Also, skin anesthesia was tested by sensitivity to pin prick, but never until after the fifth day, so as not possibly to influence the patients' requirements of morphine. Subjectively, the patients' volunteered remarks concerning a comparison of the discomfort encountered during the various procedures were noted, and, further, the patients were questioned on this point after complete recovery had occurred. The patients were never told that they had

From the Department of Surgery, North Carolina Baptist Hospital and Bowman Gray School of Medicine of Wake Forest College, Winston Salem, N. C., and the Western North Carolina Sanatorium, Black Mountain, N. C.

received anything at the time of the operation for the relief of pain.

METHOD OF USE

Intercostal nerve blocking at the time of operation is usually quite simple. The nerve runs in a shallow groove on the inferior margin of the corresponding rib. Thus, with the chest open, by palpating the pleural surface of the rib with one hand, and the inferior margin of the rib with the needle tip, the injected solution can be accurately placed. If a nerve is actually exposed during resection of the rib, then the nerve can be directly injected. One cubic centimeter of efocaine per nerve is sufficient; the nerve or nerves corresponding to the resected rib or ribs are injected, with the two immediately adjacent nerves above and below. For relief of pain other than operative, percutaneous injection is used, with the usual technique of intercostal block being followed, but 2 cubic centimeters of solution are used to insure adequate contact with the nerve. The solution must be placed accurately, as very little diffusion occurs. If the patient is not anesthetized, then procaine anesthesia should be first induced to prevent the sudden but short lasting stinging pain that occurs when efocaine is injected into unanesthetized tissue.

MODE OF ACTION

The active ingredients of efocaine are procaine (1 per cent), procaine hydrochloride (0.25 per cent), and butyl-p-aminobenzoate (5 per cent). The solvent is a mixture of polyethylene glycol-300 and propylene glycol, with phenyl mercuric borate (1:25,000) added for a preservative. When this solution comes in contact with the tissue fluids the active ingredients, being only slightly soluble in water, are precipitated out to form a crystalline depot (the solvent is rapidly absorbed). The crystalline depot is slowly absorbed over a period of days, providing a local anesthetic action until it is absorbed. Any nerves bathed by the absorbing fluid are completely blocked. Mannheimer has reported that efocaine causes severe nerve destruction in animals, and believes that the beneficial action of efocaine is due to the actual nerve destruction. Hall apparently concurs in this belief. However, Weinberg found that "the subcutaneous, intramuscular and perineural injection of efocaine produces no significant permanent damage to the tissues involved and is of the same order as that seen following the injection of procaine." Clinical results indicate the validity of Weinberg's experimental results. It is known that regenerating nerve fibers grow at a rate of approximately 2 millimeters daily. The average length of anesthesia following efocaine blockage of intercostal nerves is 15 days. The intercostal nerves in even a small woman are approximately 30 centimeters long. Thus, if a nerve was destroyed and wallerian regeneration occurred, as Mannheimer says does occur, anesthesia should persist for 150 days! This has not been observed.

RESULTS

Eighty-four patients having a single operative procedure (such as lobectomy, pneumonectomy, esophageal resection, ligation of patent ductus arteriosus, decortication) had an efocaine block induced during the procedure. Of these eighty-four, 65 had a satisfactory result, as judged by the patients' analgesic requirements, early mobility, acquiescence when requested to cough, skin anesthesia, and general well being. The average morphine requirement for this group of patients was 17 milligrams per 24 hours for the first 96 hours postoperatively. The other 19 patients were judged to have a less than satisfactory result; each patient in this classification received an average of 115 milligrams of morphine in the first 96 hours, or 29 milligrams per 24 hours.

Sixteen patients had at least 2 thoracic operations each, for a total of 38 operations. Efocaine intercostal block was induced on each patient during at least 1 procedure, for a total of 18 procedures. The daily requirement of morphine per patient per day, following the procedures accompanied by the intercostal block, was 18 milligrams. The average daily requirement of morphine for the control patients was 33 milligrams.

An area of skin anesthesia was obtained in every patient on whom efocaine was used. However, in the "unsatisfactory result" cases the area was often incomplete, being confined, for example, to an area of skin below or above

the incision. In the successful cases, the anesthetic area included a band of skin 12 to 15 centimeters wide centered on the incision.

The duration of skin anesthesia varied from 10 to 26 days, with an average of 15.2 days. Puderbach and Shaftel noted an average duration of anesthesia of 14.2 days, following efocaine intercostal block to relieve upper abdominal postoperative pain.

No complications in any way related to the use of efocaine have been observed.

DISCUSSION

The evaluation of the efficacy of various drugs to relieve postoperative pain is a process fraught with pitfalls. Patients always expect pain; other patients, as well as well meaning relatives and friends, have warned of pain that will follow any operation. Postoperatively, both the nursing and house staffs inquire solicitously as to the amount of pain that is present. It would take a stoic of no mean degree to withstand the psychologic impact of such multiple suggestions. The skin anesthesia that goes with a successful intercostal block affords an objective measure of testing the efficacy of the block, regardless of the presence of pain. The patients with excellent results had good skin anesthesia in every case. Those with less than excellent results usually had incomplete areas of anesthesia, but at times a patient with an excellent area of anesthesia would require a maximum of analgesics.

Blades and Ford, in evaluating the effectiveness of repeated novocain intercostal blocks administered via indwelling plastic tubes, found that the subjective benefits were more impressive than the reduction of amount of analgesics necessary. It is interesting to note that in their series of 36 patients, the ratio of morphine required by treated patients (1,823 mgm.) to morphine required by a similar number of control patients (2,959 mgm.) is 60 per cent. In the present study this ratio is 58 per cent, thus seemingly indicating that either method offers approximately the same degree of pain reduction. It also appears that it may be impossible to alleviate completely the need for analgesics, even with a 100 per cent effective block. Further evidence for this concept is found in the analgesic requirements of 2 patients each of whom had a malignant tumor involving the chest wall. Both patients, preoperatively, were having severe pain, but secured complete relief with percutaneous efocaine block of the involved intercostal nerves. At operation in each case a portion of the chest wall was resected, and the intercostal nerves that innervated the affected segments were divided. Nevertheless, analgesics were required postoperatively to practically the same extent (an average of 17.5 mgm. per day for the first 4 days) as for the patients who had had a successful postoperative block.

Each of the cases of unsatisfactory result fell into one of three categories: (1) Second or third stage thoracoplasties, or Schede thoracoplasties. In such operations it is impossible to localize accurately the nerves that correspond to the previously resected ribs; thus, accurate placement of the anesthetic solution is impossible to achieve. (2) Failure to inject a sufficient number of nerves (at least 2) above and below the immediately affected nerve. (3) Drainage tubes inserted through an interspace outside of the anesthetized area.

SUMMARY

It appears that efocaine block of the pertinent intercostal nerves will afford approximately a 50 per cent reduction in the amount of analgesic required after thoracotomy. The relief obtained is of the magnitude afforded by continuous procaine infiltration via indwelling plastic tubes or by actual surgical interruption of the intercostal nerves.

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THE DEPOSITION OF RADIOPHOSPHORUS IN FRACTURED BONES IN RATS

G. W. WILKINSON, M.D., and C. P. LEBLOND, M.D., Ph.D., Montreal, Canada

RADIOPHOSPHORUS may be used to study the formation of the mineral components of bone. Work with this isotope is greatly facilitated by the combined use of radioautography and Geiger counting (5). In the present investigation, these two methods were used jointly in a study of bone regeneration after fracture.

The essential change observed after fracture was an increased uptake of radiophosphorus, readily detected by Geiger counting. Radioautographs revealed that this uptake was due at least partly to the calcification of new bone trabeculae appearing at the fracture site.

In addition, observations made in intact areas of the bone revealed the existence of an increased uptake of radiophosphorus which was not associated with radioautographically visible deposition. This phenomenon is attributed to a widespread reconstruction of bony tissue, extending even to nonfractured bones.

METHODS

A closed, complete fracture of the left humerus and an open incomplete fracture of the left tibia were made in each one of a series of male rats weighing 50 ± 5 grams. The animals were anesthetized with ether and tied to an operating board. The complete fracture of the left humerus was produced by grasping the foreleg between the fingers and thumb of both hands and snapping the bone at its midportion. The incomplete fracture of the left tibia was carried out as follows: the skin over the left tibia was cleaned with 70 per cent alcohol, and a short vertical incision made over the anterior surface near its midpoint. The muscles were retracted to expose the tibia. With a dental mandril, a transverse cut was made through the bone until the bone marrow was reached. The skin was then closed with No. 2 cotton sutures. Recovery was satisfactory. The day after operation, the animals were limping about their cages and eating normally. All animals received 200 microcuries of radiophosphorus by subcutaneous injection 4 hours before sacrifice.

Specific activity measurements. Groups of 2 rats each were sacrificed at 1, 4, 8, 12, and 19 days after fracture. Both the normal and fractured humeri and tibias were removed. The diaphyses were separated from the epiphyses in such a way that the epiphysial plate was included with the corresponding epiphysis. In both epiphysis and diaphysis, a determination of the amount of radiophosphorus per milligram of total phosphorus was determined. This involved a measurement of radioactivity and a determination of total phosphorus, both operations requiring a previous digestion of the bone parts with 2 cubic centimeters of concentrated nitric acid and 1 drop of 30 per cent hydrogen peroxide. The test tubes were heated in a water bath until a dry white residue remained. (Control experiments confirmed that phosphate was quantitatively recovered by this method.) The residue was dissolved in 5 per cent trichloroacetic acid. An aliquot was used for direct estimation of the radioactivity in a crucible placed under the Geiger counter. Another aliquot was used for the colorimetric determination of phosphorus by the method of Fiske and Subbarow. Since the trichloroacetic acid evaporates quickly, the containers had to be tightly covered until the work was completed. Specific activity was expressed as per cent of injected dose per milligram of phosphorus.

Radioautographs. A group of 6 animals treated as described above were sacrificed at 4 days after fracture. A few other similar animals were sacrificed 1, 2, and 8 days after fracture. The bones were fixed in a mixture of 75 per cent alcohol and 25 per cent commercial formalin, embedded in celloidin without previ-

From the Department of Anatomy, McGill University, Montreal, Canada. This work was supported by a grant from the Defence Research Board, Department of National Defence, Canada.

TABLE I.—SPECIFIC ACTIVITIES OF DIAPHYSES AND EPIPHYSES OF FRACTURED LEFT HUMERI AND INTACT RIGHT HUMERI IN 45 TO 55 GRAM RATS WHICH, AT VARIOUS TIME INTERVALS AFTER FRACTURE, RECEIVED AN INJECTION OF CARRIER-FREE RADIOACTIVE PHOSPHORUS AND WERE SACRIFICED 4 HOURS LATER

Time after fracture	Intact humeral diaphysis		Fractured humeral diaphysis		Epiphysis of intact humerus		Epiphysis of fractured humerus	
	s.a.	Diff. from normal	s.a.	Diff. from normal	s.a.	Diff. from normal	s.a.	Diff. from normal
1 day	0.06	—0.02	0.10	0.02	0.16	—0.04	0.17	—0.03
	0.14	0.06	0.18	0.10	0.53	0.33	0.24	0.04
	0.16	0.08	0.19	0.11	0.51	0.31	0.36	0.16
	0.15	0.07	0.22	0.14	0.42	0.22	0.62	0.42
Averages	0.13	0.05	0.17	0.09	0.40	0.23	0.35	0.15
4 days	0.26	0.18	0.40	0.32	0.66	0.46	0.78	0.58
	0.20	0.12	0.33	0.25	0.61	0.41	0.62	0.42
	0.16	0.08	0.34	0.26	0.49	0.29	0.62	0.42
	0.45	0.37	0.52	0.44	0.24	0.04	0.53	0.33
Averages	0.27	0.19	0.40	0.32	0.50	0.30	0.64	0.44
8 days	0.21	0.13	0.22	0.14	0.28	0.08	0.27	0.07
	0.15	0.07	0.23	0.15	0.40	0.20	0.54	0.34
	0.10	0.02	0.26	0.18	0.32	0.12	0.40	0.20
	0.11	0.03	0.25	0.17	0.31	0.11	0.45	0.25
Averages	0.14	0.06	0.24	0.16	0.33	0.13	0.41	0.22
12 days	0.11	0.03	0.13	0.05	0.28	0.08	0.24	0.04
	0.10	0.02	0.20	0.12	0.22	0.02	0.38	0.18
	0.13	0.05	0.25	0.17	0.36	0.16	0.40	0.20
Averages	0.11	0.03	0.19	0.11	0.29	0.09	0.34	0.14
19 days	0.05	—0.03	0.12	0.04	0.18	—0.02	0.17	—0.03
	0.09	0.01	0.10	0.02	0.28	0.08	0.27	0.07
	0.01	—0.07	0.05	—0.03	0.08	—0.12	0.07	—0.13
	0.00	—0.02	0.22	0.14	0.23	0.03	0.21	0.01
Averages	0.05	—0.03	0.12	0.04	0.19	0	0.18	—0.02

ous decalcification, sectioned and coated with photographic emulsion according to a previously described method (4).

RESULTS

The *specific activities* of bone parts at various times after fracture are reported in Tables I and II. The results obtained with the humeral diaphyses (where complete fractures were performed) are illustrated in Figure 1. Each dot indicates the specific activity observed in 1 humeral diaphysis, a solid black dot corresponding to a fractured bone and a double-ringed dot, to an intact bone. The two dots of each animal are connected by a broken line. In addition, the upper solid line joins the mean values for the specific activities of the fractured bones at the various time intervals. The lower solid line joins the corresponding values for the intact bones.

The most obvious result is that the specific activity of every single fractured humeral diaphysis was higher than that of the corresponding intact bone. The differences were slight 1 day after fracture, but large at later times. Statistical analysis of paired results by Student's method revealed that the difference between fractured and intact humeral diaph-

TABLE II.—SPECIFIC ACTIVITIES OF DIAPHYSES AND EPIPHYSES OF FRACTURED LEFT TIBIAS AND INTACT RIGHT TIBIAS IN 45 TO 55 GRAM RATS WHICH, AT VARIOUS TIME INTERVALS AFTER FRACTURE, RECEIVED AN INJECTION OF CARRIER-FREE RADIOACTIVE PHOSPHORUS AND WERE SACRIFICED 4 HOURS LATER

Time after fracture	Intact tibial diaphysis		Fractured tibial diaphysis		Epiphysis of intact tibia		Epiphysis of fractured tibia	
	s.a.	Diff. from normal	s.a.	Diff. from normal	s.a.	Diff. from normal	s.a.	Diff. from normal
1 day	0.08	0.03	0.09	0.04	0.28	0.10	0.23	0.05
	0.17	0.12	0.15	0.10	0.50	0.32	0.51	0.33
	0.11	0.06	0.14	0.09	0.43	0.25	0.68	0.50
	0.17	0.12	0.23	0.18	0.49	0.31	0.56	0.38
Averages	0.13	0.08	0.15	0.08	0.42	0.25	0.49	0.32
4 days	0.17	0.12	0.34	0.29	0.48	0.30	0.43	0.25
	0.16	0.11	0.19	0.14	0.46	0.28	0.51	0.43
	0.20	0.15	0.30	0.25	0.46	0.28	0.42	0.24
	0.32	0.27	0.52	0.47	0.59	0.41	0.76	0.68
Averages	0.21	0.16	0.34	0.29	0.50	0.32	0.53	0.40
8 days	0.11	0.06	0.16	0.11	0.44	0.26	0.42	0.24
	0.17	0.12	0.12	0.07	0.43	0.25	0.41	0.23
	0.07	0.02	0.26	0.21	0.37	0.19	0.41	0.23
	0.07	0.02	0.29	0.24	0.34	0.16	0.34	0.16
Averages	0.10	0.06	0.21	0.16	0.39	0.22	0.39	0.22
12 days	0.04	—0.01	0.17	0.12	0.35	0.17	0.36	0.18
	0.04	—0.01	0.11	0.06	0.23	0.05	0.27	0.09
	0.08	0.03	0.29	0.24	0.43	0.25	0.39	0.21
Averages	0.05	0	0.19	0.14	0.34	0.16	0.34	0.12
19 days	0.04	—0.01	0.05	0	0.15	—0.03	0.17	—0.01
	0.07	0.02	0.36	0.31	0.33	0.15	0.44	0.26
	0.01	—0.04	0.04	—0.01	0.07	—0.11	0.07	—0.11
	0.05	0	0.04	—0.01	0.20	0.02	0.15	—0.03
Averages	0.04	—0.01	0.10	0.08	0.19	0.01	0.21	0.03

yses was statistically significant. There is, therefore, a greater uptake of radiophosphorus by the fractured than by the intact bone. (In the tibia, the difference between saw-cut fractured and intact diaphyses was on the verge of significance.)

The greatest uptake of labeled phosphate was observed at 4 days after the fracture in the diaphyses of both humeri (Fig. 1, Table I) and tibias (Table II). At later time intervals, there was a slow decline in the avidity of the fractured bones for phosphate (Fig. 1). While there were no normal controls in this experiment, unpublished work had shown that the normal specific activities of the diaphyses of humerus and tibia at 2 hours after injection averaged 0.08 and 0.05 respectively. A return to such values was observed at 19 days in 3 of the 4 tibial diaphyses with saw-cut fractures (Table II), but only in 1 of the 4 humeral diaphyses with complete fractures (Table I).

Surprisingly, the intact diaphyses symmetrical to the fractured ones also showed a greater avidity for labeled phosphorus than normally, with a maximum P^{32} uptake also at 4 days after fracture (Fig. 1). By 19 days, however, the intact diaphyses had returned to normal values (Tables I and II).

The same pattern was distinguishable in the epiphyses, with the P^{32} uptake being increased

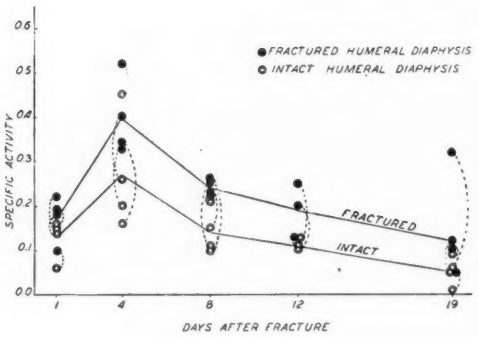

Fig. 1.

on both the fractured and intact sides (Tables I and II). It may be concluded that fractures produce an increase in phosphorus uptake by the epiphyses and diaphyses of intact as well as of broken bones.

The *radioautographs* of fractured bones were then compared with those of the intact bones. The intact bones showed no obvious differences from the usual pattern of P^{32} uptake. The midportion of the shaft previously referred to as the "cylinder" (5) showed a deposition of radiophosphorus on the periosteal surface. The funnel-like subepiphysial regions previously referred to as the "funnels" showed a deposition of radiophosphorus on the endosteal surface. The bony spicules on the shaft side of the epiphysial plate showed the most intense reaction, while those in the epiphysis proper showed a moderate reaction. There was no evidence that any of these reactions differed in intensity from those previously described in normal growing rats. It was concluded that the formation of new bone continued in the intact limb.

In the fractured bones, the epiphysial and "funnel" regions also showed apparently normal reactions: an intense blackening on the shaft side of the epiphysial plate (Figs. 3 and 4), a moderate reaction on the bone spicules in the epiphyses (Figs. 2 and 3) and an endosteal deposition of P^{32} in the funnel-like subepiphysial region (Figs. 3 and 4).

The "cylinder" region, where the fractures were produced, showed changes characteristic of fractures. At 1 day after the trauma, nothing abnormal was recognized. By 2 days (Fig. 2), there was an increase in the periosteal (*P*) and endosteal (*E*) deposition of radiophosphorus. Histologic examination of the periosteum showed a rounding up of the normally flat osteoblasts (the "cambium layer" of Enneking), as well as an increase in their number. Occasionally, small masses giving a strong radioautographic reaction appeared between the osteoblasts. At 4 days, this periosteal material had blossomed into numerous trabeculae of young bone covered with osteoblasts and giving an intense autographic reaction. These bone trabeculae (variously described by previous authors as "osteoid," "osteogenic growth," "new bone") stand out on the radioautographs due to their intense uptake of radiophosphorus (Figs. 3, 5, and 6). Such periosteal proliferation is abundant not only in complete (*PP*, Fig. 3), but also in saw-cut, fractures (Fig. 5), often extending to a considerable distance from the site of fracture and sometimes even covering the whole length of the shaft (Fig. 6). However, periosteal proliferation is at a minimum in the immediate vicinity of the fracture site (Figs. 5 and 6). Finally, the periosteal proliferation did not usually extend along the outside walls of the funnel (Figs. 4 and 6). An exception to this rule may be seen in the lower left of Figure 3.

Occasionally, some proliferation of bone trabeculae from the endosteum was seen (Fig. 3). These endosteal trabeculae also fixed P^{32} intensely. When present, they were usually limited to the fracture site.

It may be noted that fragments detached from the bone by the trauma may continue to deposit P^{32}. Small reactive fragments may be seen in the bone marrow in the lower portion of Figure 4 and at the fracture site in Figure 5. Similar observations were made on a few radioautographs at later time intervals. (This result lends some support to the practice of using bone chips in fracture treatment.)

DISCUSSION

The radioactive phosphorus incorporated into bone within a certain time interval may be considered to consist of at least two fractions; (1) the phosphate used to make up the crystals of bone built during that time, and (2) the phosphate introduced onto the surface

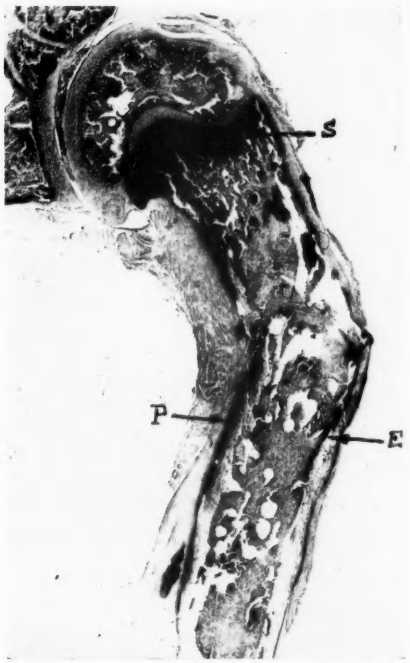

Fig. 2.

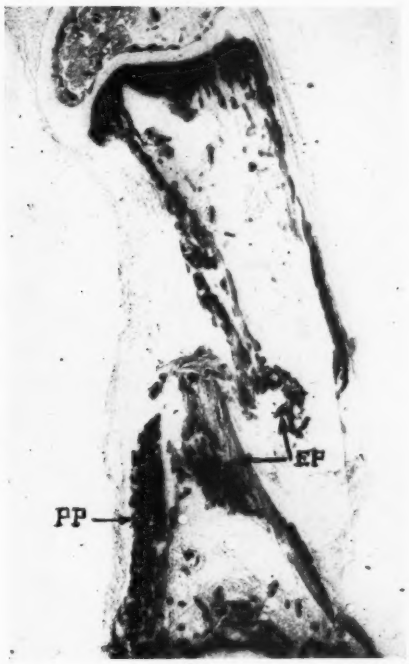

Fig. 3.

Fig. 2. Coated radioautograph of humerus 2 days after complete fracture; safranine stain. The reactions of the head of the humerus and epiphysial plate visible in the upper part of the picture are the same as in intact control animals. In addition, there is an unusually intense deposition of P^{32} in some areas of periosteum (*P*) and endosteum (*E*). This is taken to be a consequence of the fracture.

Fig. 3. Coated radioautograph of humerus 4 days after complete fracture; unstained. The reaction of the head of the humerus and epiphysial plate are the same as usual. Trabecular bone fixing radiophosphorus intensely has formed in the region of the periosteum (*PP*) and extends over most of the shaft. This periosteal response is missing near the point of contact of the two bone parts. Trabecular bone fixing radiophosphorus intensely has also formed from the endosteum (*EP*). This material plugs the marrow cavity near the fracture site in the lower bone fragment.

of the pre-existing crystals by the process of iso-ionic exchange. In the present work, the role of exchange appeared from the outset to be negligible. In young animals crystal surfaces are readily accessible for exchange with the circulating phosphate, and there was no reason to doubt that this was equally true in fractured limbs. It was, therefore, assumed that the variations in P^{32} uptake observed in this work could not be explained by considerations of exchange but rather were due to variations in the amount of new crystalline material present. In order to find out whether the results could be explained on this basis, the fractured diaphysis and other parts of the bones had to be considered separately.

Fractured diaphysis. Counts of radioactivity in the fractured diaphyses of both tibias and humeri showed an increase in the uptake of radiophosphorus as compared with the intact limbs (Fig. 1, Tables I and II). A similar increase in P^{32} uptake by fractured bones was also observed by Bohr and Sørensen and by Ruf. Here, the increase was detectable 1 day after the fracture (Fig. 1), although no unusual phosphate deposition was seen on the radioautographs at that time. The increase in phosphate uptake was more pronounced at 4 days after fracture (Fig. 1). Radioautographs at 2 and especially 4 days showed areas of intense reaction which proved to consist of trabeculae of new bone arising in

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 4. Coated radioautograph of tibia 4 days after saw-cut fracture; unstained and slightly overexposed. The site of fracture is immediately below the picture. The autograph shows from the top down the pronounced epiphysial reaction and the endosteal reaction of the funnel (*E*) characteristic of normal animals. Trabecular bone formation may be recognized in the periosteal region of the lower part of the figure as a thick reacting area on either side of shaft (*P*). (Light circles are artefacts of emulsion.)

Fig. 5. Coated radioautograph of cylindrical portion of tibia 4 days after a saw-cut fracture. The site of fracture is visible slightly above the center of the picture and on the left. The trabecules of new periosteal bone are well developed everywhere, except across the bone from the site of fracture. A few broken fragments at the site of fracture have given rise to small bone trabeculae which show an autographic reaction.

Fig. 6. Coated radioautograph of tibia 4 days after an attempted saw-cut fracture which resulted in a complete fracture. The new periosteal bone shows an intense reaction which extends around most of the shaft, except in the upper and lower funnel. The endosteal reaction is minimal.

periosteal and endosteal areas. The presence of P^{32} in these trabeculae at 4 days (Figs. 3, 5, and 6) may well explain the peak of P^{32} uptake observed with the Geiger counter at that time (Fig. 1).

The role played by the new trabeculae of *periosteal* bone in the repair of fractures is not obvious. Their intense radioautographic reaction indicates that they calcify as soon as they are formed; and therefore, they must soon be hard enough to play a role in strengthening the fractured bone. Thus, when the bone trabeculae spread along most of the shaft to form a tube around the diaphysis (Figs. 5 and 6), they would thus reinforce the original bone and, at least in complete fractures, serve as an anchorage on either side of the break for the final bone jacket which fastens the two fragments. (This bone jacket is usually formed by ossification of the cartilage callus appearing in the gap.) The new trabeculae of endosteal bone, which are usually limited to a small area of the medullary cavity close to the site of fracture, may also play a role in strengthening the gap.

Behavior of nonfractured parts of bones. The increase in P^{32} uptake was not limited to the fractured diaphysis, but extended to the epiphysis of the fractured bones and also to the intact bone symmetrical to the fractured one.

In all these areas, the increase in specific activity was often considerable, particularly 4 days after fracture when the amounts of radioactivity were sometimes 2 or 3 times greater than under normal conditions (Tables I and II). To explain this surprising uptake of radiophosphorus in the intact areas of bone, examination of radioautographic pictures was of little help, as they simply showed that these intact areas of bone reacted as usual. Thus, the epiphysis of the fractured bone continued to show the pattern of growth found in normal bone, especially in the region of the epiphysial plate, and immediately below. Similarly, the uptake of radiophosphorus by the periosteum of the nonfractured bone appeared to be normal. Thus, there was no visible deviation from the normal pattern of P^{32} deposition. The problem was to explain how, under such conditions, a large increase in radiophosphorus may take place. Perhaps, new crystal material is formed throughout the bone, since no specific localization would then be apparent on radioautographic pictures! Such a phenomenon might be the result of the action of mechanical factors.

Theoretic and experimental support has been presented (3) for the view that "pressure" produces bone resorption (while a negative pressure or tension results in bone growth). Pressure would have a direct physical effect on the solubility of bone crystals. This effect (presented in a mathematical form elsewhere, 3) implies that, when subjected to pressure, a crystal will dissolve even if kept in a saturated solution. It is likely that, under biologic conditions also, bone crystals subjected to pressure will dissolve.

This hypothesis explains the data obtained by Roche and Mourgue in rats with fractures (6, 7). These authors found a moderate decrease in phosphate content in both the fractured bone and the corresponding intact bone. This was apparent up to 21 days after fracture, after which time there was a return to normal values. The decreased phosphate content in the intact bone implies a dissolution of some of the crystals. This in turn may be due to the increased pressure which the animals bring to bear on the intact limb due to disuse of the fractured limb.

Such a simple explanation does not account for the whole picture. Thus, in the present work there was also an increased uptake of P^{32} in the intact limbs. Formation of new crystal material must have taken place.

This also may be explained on the assumption that the pressure bearing on the intact limb is increased as a result of the fracture, or merely that the direction of this pressure has changed. New points of high pressure will appear in the bone, and crystal dissolution will occur there. As pressed crystals dissolve, the interstitial fluid tends to become supersaturated with respect to the crystals not subjected to pressure. The supersaturation will be reduced by growth of these unpressed crystals. The crystalline material deposited in the course of this process will consist not only of the dissolved crystal ions, but also of circulating interstitial phosphate, so that if P^{32} is present it will be included. Thus, an increased specific activity will be observed in the intact limb.

It is concluded that after fracture, there is dissolution and reprecipitation of crystalline material, not only in the fractured bone but also in intact bones far from the seat of injury. A fracture may thus produce an extensive reconstruction of the skeleton.

SUMMARY

Fifty gram male rats were subjected to a complete fracture of the humerus and a sawcut fracture of the tibia, both being placed in the midportion of the shaft. At various time intervals after fracture, the animals were given an injection of P^{32} and sacrificed 4 hours later. The radioactivity of the bones was localized by means of radioautography and quantitatively estimated by Geiger counter measurements.

Radioautographs showed that the trabeculae of new bone which appear 2 to 4 days after fracture fix radiophosphorus most actively (Figs. 3, 5, and 6). Therefore, these trabeculae must calcify rapidly and soon play a role in strengthening the fractured bone.

Geiger counter measurements revealed that the uptake of radiophosphorus was increased, not only in the diaphysis but also in the epiphyses of the fractured bone, and even in the contralateral intact bone (Fig. 1). These

findings are explained by a reconstruction of bony tissue extending to bones other than those fractured. This reconstruction is attributed to changes in internal bony pressures, which in turn are due to changes in the positions and use of body and limbs after fracture (3).

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RADICAL GASTRECTOMY FOR BENIGN GASTRIC ULCER

ALLEN M. BOYDEN, M.D., Portland, Oregon

THE DISCOURAGING 5 year survival rate in patients with carcinoma of the stomach has led to increasing interest in formulating a more adequate attack against this disease. Earlier diagnosis is of the greatest importance. However, because of the vagueness and often complete lack of symptoms in the early stages, the majority of patients still present themselves for treatment after the lesion is advanced. It would seem necessary, therefore, to consider more aggressive surgical treatment if improvement in end results is to be forthcoming.

Although gastrectomy was one of the early surgical operations within the abdomen, and is still one of the most common, it is strange that surgeons have failed to apply the same principles in attacking carcinoma of the stomach that they have long agreed upon when approaching malignant lesions elsewhere in the body. For example, it is unthinkable that simple mastectomy should be performed in operable cases of carcinoma of the breast. Yet "simple" subtotal gastrectomy has been practiced for years by the majority of surgeons in their planned attack upon obvious carcinoma of the stomach. Despite the writings and teachings of such men as Coller, Wangensteen (24), Lahey (13), Ochsner, and Pack and McNeer, "radical" gastrectomy, subtotal and total, is not the usual practice even today. The lymphatic drainage of the stomach is still commonly ignored.

The probable reasons for this are several. Undoubtedly, the most important one is the fact that subtotal gastrectomy is the accepted surgical treatment for duodenal and benign gastric ulcer. Since these are common surgical lesions and since the consideration of lymphatic drainage has no bearing in their treatment, the habit of simple partial gastrectomy is continually being strengthened. Once acquired, this habit is perhaps difficult to break when carcinoma of the stomach is encountered. That such a limited technique is a prevalent practice is confirmed by McNeer and his associates in their study of resection survivors eventually coming to autopsy.

Furthermore, the lymphatic drainage of the stomach is complex. The lymphatics of the stomach drain into all of its attached and supporting omenta and ligaments instead of in one direction as, for example, the lymphatic drainage of the cecum and ascending colon into their adjacent mesentery. This makes en bloc dissection more difficult. In addition, the common attitude of relative hopelessness of cure in malignant lesions of the stomach has led to the common practice of removing the primary lesion, "picking out" the obviously involved adjacent lymph nodes and "calling it a day." When it is realized that at least 75 per cent of gastric carcinomas resected with hope of cure have already metastasized to lymph nodes as shown by Coller and his associates, is it any wonder that so few patients survive 5 years? Obviously, any increase in the percentage of 5 year survivors must result from more aggressive surgical attack based on anatomic and pathologic facts as they pertain to the disease.

The earliest carcinomas coming to operation are the gastric ulcers which prove to be malignant. Since it is admittedly difficult, and often impossible, to determine malignancy from examination preoperatively or at the operating table as shown by Allen and Welch, Lahey (10, 11), Ransom and Wangensteen (23), the majority of the malignant ulcers are treated completely inadequately as far as removal of the lymphatic spread is concerned. The common surgical practice for gastric ulcer is simple removal of the lower two-thirds of the stomach. For the ulcer proving to be malignant such an operation is entirely comparable to removing the cecum for carcinoma without resecting the right mesocolon. This is indeed an unfortunate situation. Incomplete operation is performed for the earliest lesions, a high percentage of which should be curable, whereas extensive en bloc resection is reserved for the advanced cancers

Fig. 1. Roentgenogram showing lesser curvature "ulcer" which proved on microscopic examination to be primary adenocarcinoma (Case 1).

in which the possibility of cure is pitifully small.

Since 1940, it has been my policy to perform radical subtotal gastrectomy in all obvious or suspected malignant cases, the determination being made at the time of exploration. Approximately 3 years ago, 2 malignant ulcers of the lesser curvature were misinterpreted as benign, and inadequate operation was performed. No gross glandular metastases were found. In each instance the diagnosis of carcinoma was returned 2 days later. Both of these patients are dead.

The first patient died 2½ years postoperatively of recurrent carcinoma. At operation a 1.5 centimeter indurated area was palpable along the lesser curvature about 5 centimeters above the pylorus. This coincided with the site of the "ulcer" seen at x-ray examination, the roentgenologist having considered the possibility of carcinoma (Fig. 1). To be certain that this actually represented a lesion, the stomach was opened and a small superficial ulcer found. Simple partial gastrectomy was done. Figure 2 shows a photograph of the fresh specimen. It was considered benign on gross inspection by the pathologist and a frozen section was not made. Figure 3 is a photomicrograph of this ulcer. It is an ulcerating, primary adenocarcinoma which does not penetrate through the muscular wall.

The second patient died 15 months postoperatively with massive lymphatic extension of carcinoma. In this case a grossly benign ulcer of the lesser curvature at the angulus was found and partial gastrectomy performed. The microscopic evidence of malignancy in the surgical specimen was evident at only one point in the margin of a peptic ulcer and was confined to a small area of the submucosa and inner muscular layer of the gastric wall (Fig. 4). Radical subtotal resection certainly would have offered both of these patients a greater chance of recovery.

Since this experience I have elected to perform radical subtotal gastrectomy for all gastric ulcers encountered at exploration. Quite obviously it is impossible to prove the efficacy of this mode of attack at this date. It will take the cumulative experience of many surgeons following this reasoning 5 or 10 years to reveal the effect it may have on the survival rate of patients with malignant ulcers. However, it would seem more logical to treat the early lesions radically than to expect real dividends in 5 year cures by wide resection of adjacent organs in far advanced lesions. Such a program would preclude the grossly incomplete treatment of the early malignant ulcer.

CLINICAL MATERIAL

The records of all patients operated on at The Portland Clinic for gastric ulcer and carcinoma during the 6 years from January 1946 to January 1952 have been reviewed in the hope that their perusal might shed some light on this problem. During this interval 70 patients with gastric ulcer have come to operation. Table I shows the operative procedure and the operative mortality. Pathologic examinations were made in 66 cases (eliminating 3 cases of perforated ulcer and 1 of vagotomy and gastroenterostomy). Eight of these lesions or 12.1 per cent were found to be malignant. The 1 postoperative death occurred in a patient with a juxtaesophageal ulcer who was

Fig. 2. Resected stomach with small ulcer considered benign at gross inspection by surgeon and pathologist but proving on microscopic examination to be a primary adenocarcinoma (Case 1).

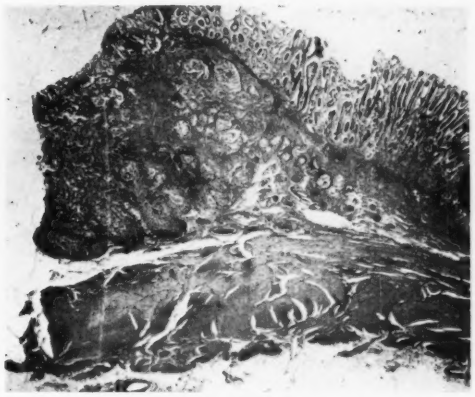

Fig. 3. Case 1. Ulcerating adenocarcinoma of the stomach. Low power view showing one border of the ulcerating carcinoma which measured 1.5 centimeters in diameter. While the tumor has invaded numerous lymphatic spaces, it is confined to the mucosa and submucosa and the muscularis is unaltered. ×7.

treated primarily by vagotomy. The ulcer failed to heal. Esophagogastrectomy was performed because the ulcer was thought to be malignant. Death resulted from leakage at the suture line and empyema.

Review of the x-ray findings and preoperative diagnoses in these patients yields most interesting information. In the group of cases of benign ulcer, the x-ray diagnosis was carcinoma in 6, and malignancy was questioned in 19 others, a total inaccuracy of 42.4 per cent. Furthermore, the preoperative diagnosis or opinion at the operating table was carcinoma in 6 and malignancy was questioned in 10 others, an inaccuracy of 27.1 per cent. In 2 of these patients transverse colectomy was performed along with partial gastrectomy because of apparent invasion of the mesocolon.

Of the 8 malignant lesions, 6 were thought at operation to be benign. One of these was reported by the pathologist to be benign on frozen section, the final microscopic diagnosis being carcinoma arising in a peptic ulcer.

X-ray studies were made in 7 of these 8 patients. Barium study was not done on the remaining patient because operation was carried out for perforation. The diagnoses were as follows: carcinoma, 1; question of malignancy, 2; benign ulcer, 2 (1 a marginal ulcer); and no ulcer, 2 (in 1 case there was pyloric obstruction, in the other no abnormality at 6 barium studies by 3 roentgenologists).

The site of ulceration in the benign group is depicted in Figure 5. Thirty-three ulcers were found on the lesser curvature, 5 being high or juxtaesophageal; 24 in the pyloric and prepyloric area; 4 on the posterior wall; and 1 on the greater curvature.

Figure 6 shows the location of the malignant ulcers. Two were in the prepyloric area, 2 on the lesser curvature, 2 in the anterior wall, 1 on the greater curvature, and 1 was a marginal ulcer near the stoma following resection.

It is apparent that one cannot depend on the location of the ulcer in making the determination of benignancy or malignancy. The malignant potentiality of greater curvature ulcers is well known. Holmes and Hampton have pointed out the great danger of malignancy in prepyloric ulcers. The incidence of malignancy in ulcerations of the lesser curvature has varied in different reports, but probably approaches 10 per cent. It was 13.7 per cent in the series reported by Marshall and Welch and 8.1 per cent in that reported by Ransom. In the present small series 5.7 per cent of lesser curvature ulcers and 7.7 per cent of prepyloric ulcers were malignant.

Fig. 4. Case 2. Adenocarcinoma in a gastric ulcer. The section shown is from one border of an ulcer crater which measured 2.3 centimeters in diameter. There is extensive fibrosis and chronic inflammation of the stomach wall. Sections through the center of the ulcer showed complete replacement of the muscularis by fibrous connective tissue. The carcinoma is confined to the mucosa and submucosa at the border of the ulcer. ×7.

TABLE I.—GASTRIC ULCER

Procedure	No. of cases	Operative mortality
Subtotal gastrectomy*	64	0
Excision of ulcer, pyloroplasty, vagotomy	1	0
Esophagogastrectomy, vagotomy	1	1
Vagotomy, posterior gastroenterostomy	1	0
Closure of acute perforation	3	0
Total	70	1

*Includes 8 malignant ulcers.

TABLE II.—CARCINOMA OF STOMACH

Procedure	No. of cases	Operative mortality	
		Cases	Per cent
Subtotal gastrectomy	38	5	13.2
Total gastrectomy	8	1	12.5
Partial esophagogastrectomy	4	1	25.0
Total resections	50*	7	14.0
Exploration and biopsy	24		
Total	74		

*Resectability rate 67.5 per cent.

The age, duration of symptoms, and free acid values were of no assistance in differential diagnosis. Reports by Marshall and Welch, and Ransom confirm these findings.

The average age of the patients with benign ulcer was 53 years, with men predominating 3 to 1.

The average age of the 8 patients with malignant ulcers was 56½ years, the oldest being 67, the youngest 38. Six were men and 2, women.

The duration of symptoms of the 8 patients with malignant ulcers varied greatly. Three had had symptoms 3 years or more, 1 for a year and a half, 1 for 1 year, 2 for 6 months, and 1 for 2 days (a perforated gastric ulcer with malignancy in its margin).

Of the patients who proved to have benign ulcer, 7 had no free hydrochloric acid and 14 others had readings of 30 units or less. The majority of the tests followed histamine injection.

Gastroscopy was performed on 13 patients with benign ulcer. The results were as follows: negative findings, 5 cases; diagnosis of malignancy, 1; probable malignancy, 3; possible malignancy, 1; benign ulcer, 3. Only 1 of the 8 patients with malignant ulcer had gastroscopy; in this case the ulcer was not visible.

The data obtained from the study of these case records corroborates that of larger series in pointing up the fact that in the individual patient it is impossible to be certain of the diagnosis until the specimen is thoroughly examined microscopically. One cannot safely depend on laboratory, x-ray, gastroscopy, or gross operative findings to rule out malignant ulcer. Neither can one be certain of a correct interpretation by frozen section.

During the last 6 years, 74 patients were operated on in The Portland Clinic for carcinoma of the stomach. These include the 8 with malignant ulcers (10.8 per cent) mentioned previously. Table II shows the type of operation and operative mortality. Twenty-four lesions were inoperable. Subtotal gastrectomy was undertaken in 38 cases, total gastrectomy in 8, partial esophagogastrectomy in 4. The operative mortality in all resections was 14 per cent. It was 13.2 per cent for subtotal resection, 12.5 per cent for total gastrectomy, and 25 per cent for esophagogastrectomy.

That attempts to carry out radical en bloc dissections did not add to this mortality is

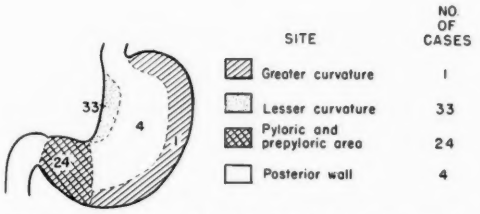

Fig. 5. Distribution of benign gastric ulcers (62 cases).

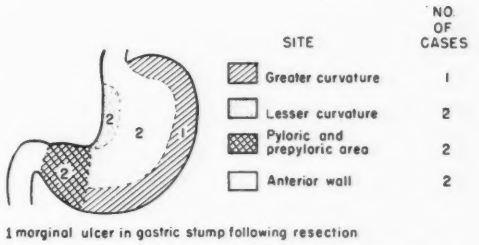

Fig. 6. Distribution of malignant ulcers (8 cases).

evident when the operative and pathologic reports are examined. Radical subtotal resections were done on 16 patients with carcinoma. Two (12.5 per cent) died, one from pulmonary embolism and one from cerebral hemorrhage. Radical total gastrectomy, including splenectomy, was performed on 3 patients with no deaths. Radical esophagogastrectomy, including splenectomy and all attached omenta of the portion of stomach removed, was done on 4 patients. One died of massive pulmonary atelectasis.

Furthermore, radical subtotal gastrectomies were performed on 11 patients proving to have benign gastric ulcers. None died. Intestinal obstruction developed postoperatively in 1 patient because a loop of jejunum had become adherent to the abdominal incision and reoperation was necessary. This is the only complication which could be attributed to the loss of the omentum.

The end results in the 8 patients with malignant ulcer are most discouraging. Six are dead of carcinoma and 1 has advanced recurrence of carcinoma. One was alive without recurrence 16 months after operation.

DEFINITION OF RADICAL SURGERY

The ideal treatment of carcinoma of the stomach, as far as cure is concerned, is total gastrectomy with excision of wide segments of the duodenum and esophagus and removal of all of the greater and lesser omenta, the gastrocolic omentum, and the spleen. Such treatment has been advocated for all gastric carcinomas by de Amesti, Lahey (12), Lahey and Marshall, Longmire and Scott and Longmire who pointed out the recent improved operative mortality in total gastrectomy.

Removal of the body and tail of the pancreas and dissection in continuity of the retroperitoneal tissue above the pancreas and on the under aspect of the diaphragm have been suggested by Allison as logical extensions of the operation of total gastrectomy in the hope of effecting cure in a higher percentage of patients. Such extensive operations necessarily carry a formidable risk. Were this the only deterrent, such procedures would receive greater favor in surgical circles. The crippling physiologic sequelae in the majority of patients undergoing total gastrectomy have led most authorities to reserve this procedure for those carcinomas involving all or most of the stomach and to compromise by recommending "radical" subtotal gastrectomy for lesions of the distal half, and partial esophagogastrectomy for lesions of the proximal portion of the stomach. Recently this attitude has been admirably expressed by Allen. Radical subtotal gastrectomy has been championed by a number of others, including Wangensteen (23, 24), Coller, and Ochsner.

Admittedly a compromise, radical subtotal gastrectomy should ideally include all of the zones of lymphatic spread demonstrated by Coller and his associates in a study of surgical specimens cleared by the Gilchrist and David modification of the Spalteholtz method (Fig. 7). It must include a wide margin of grossly uninvolved stomach above the tumor as well as a liberal cuff of duodenum. McNeer and associates have pointed out the high percentage of recurrences resulting from inadequate resections at these two margins. Coller and associates reported carcinoma extending to the proximal line of resection in 24.5 per cent and invasion of the duodenum in 26.4 per cent

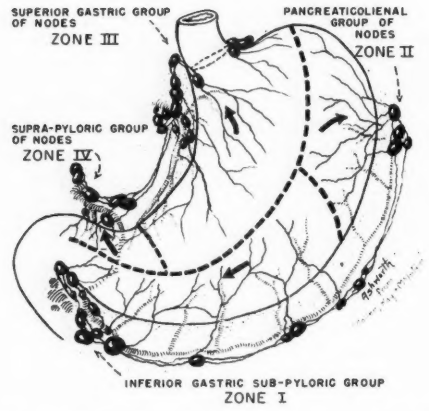

Fig. 7. Zones of lymphatic spread in carcinoma of the stomach.

of 53 cases studied. Frozen section of the upper and lower margins, though admittedly an imperfect test, if made routinely in all gastrectomies performed for malignant disease would help prevent incomplete operations.

Splenectomy has not been included in all so-called "radical" subtotal resections in the present series. The spleen has been taken only in those cases in which involvement of the area of the pedicle was grossly visible. However, the greater and lesser omenta and gastrocolic omentum have been removed with the resected stomach and the dissection commonly carried to the origin of the left gastric artery at the celiac axis (Fig. 8). The posterior peritoneum overlying the pancreas has been dissected only when gross glandular metastases were found in this area.

Radical total gastrectomy has included a wide margin of both duodenum and esophagus, all of the attached omenta, and the spleen.

Radical partial esophagogastrectomy has included the spleen and all of the omenta attached to that portion of the stomach removed. In a recent article Sweet discussed his wide experience in these cases, pointing out that en bloc excisions are much more feasible in lower esophageal and fundal lesions than in upper esophageal carcinomas.

It would be foolhardy, of course, to suggest radical total gastrectomy for patients with gastric ulcer. The addition of splenectomy to radical subtotal gastrectomy for gastric ulcer is not advocated and would seem to be unnecessarily heroic. It would undoubtedly increase the operative mortality in the large percentage proving to be benign. Furthermore, the lienal group of lymph nodes appears to be the least likely to be involved even in advanced cases of carcinoma according to Coller and his associates.

DISCUSSION

The difficulty in accurately differentiating benign from malignant ulcers is well known. The incidence of proved malignancy in patients with gastric ulcer submitted to operation is high. The actual percentage varies in different reports: Ransom, 10.1 per cent; Lempert, Waugh, and Dockerty, 13 per cent; Allen and Welch (1), 14 per cent; Graham, 17 per cent; Marshall and Welch, 19.5 per cent; Finsterer, 20.9 per cent, but is high enough in all to be alarming. In the present series 12.1 per cent were malignant.

The fact that malignant ulcers under rigid ulcer management not uncommonly become smaller or even appear to heal when viewed at intervals by x-ray is well appreciated. Because of this the majority of gastroenterologists approach the medical treatment of gastric ulcer with caution, insisting on frequently repeated x-ray follow-up examinations to denote progress. They quickly recommend operation if rapid healing fails to occur or if complete disappearance of the ulcer is not evident in a relatively short interval. Repeat barium studies frequently thereafter must prove that healing is permanent.

Because of fear of malignancy, Allen and Welch, Lahey (12), and Marshall and Welch have more recently advocated immediate operation as soon as the diagnosis of gastric ulcer is established. They feel justified in this conclusion because the operative mortality for gastric resection in their hands is negligible and the end results after subtotal gastrectomy for gastric peptic ulcer are excellent.

It would seem that whichever of these courses is followed the vast majority of malignant ulcers will come to operation at an early interval after original x-ray visualization. Following partial gastrectomy as usually per-

formed for benign disease the 5 year survival rate in these malignant ulcers proves to be much higher than in the cases of obvious gastric carcinoma. Ransom reported 41.2 per cent; Lempert, Waugh, and Dockerty 43.5 per cent; and Allen and Welch (1) 40 per cent 5 year cures in such lesions. It would seem obvious that had radical subtotal gastrectomy been undertaken in these cases the expectation of cure could have been much higher still.

Once the surgeon makes the incision the internist's dilemma is solved. The surgeon's predicament has just begun. Were it possible to determine at operation which gastric ulcers are malignant, then wide excision of the lymphatic bed could be performed in those cases. But with the stomach in his hand, the surgeon cannot tell the malignant from the benign ulcer. It is usually no more apparent to the pathologist on gross examination. Biopsy of the ulcer margin may miss the area of malignancy. Excision of the ulcer for frozen section is commonly misleading because of the difficulty of accurate interpretation by this method in this organ. Furthermore, excision of the ulcer for immediate examination is often impractical because of its location or adherence to adjacent organs. Biopsy of one or two lymph nodes is obviously inadequate. Simple subtotal resection for immediate examination by frozen section crosses the cancer field on all margins and practically precludes an adequate "clean up" of the areas of lymphatic spread should the pathologist report malignancy after examination. Not uncommonly the first inkling of the true nature of the disease comes 2 or 3 days after operation when the fixed microscopic sections are read by the pathologist. This was true in 5 of the 8 malignant ulcers herein reported.

What course then must be followed if this problem is to be solved? The surgeon may attack in a radical manner those lesions which appear to suggest malignancy. In so doing he will perform radical en bloc dissections in a large number of benign lesions (27.1 per cent of this series) and at the same time, unfortunately, may miss the early malignant lesions (6 of 8 in the present report). His only alternative would seem to be to perform radical subtotal gastrectomy in all patients operated on for gastric ulcer.

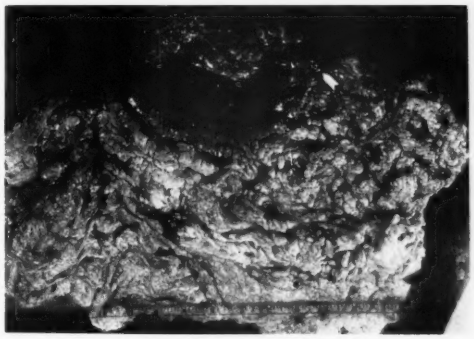

Fig. 8. Example of "radical" subtotal gastrectomy. Note attached omenta (prepyloric carcinoma).

It may be argued that such a program will apply to so small a percentage of the total cases of carcinoma of the stomach that it will have little effect on the overall survival rate. Recent Federal Security Agency statistics (4) reveal that a 2 to 5 per cent increase in the cure rate of gastric cancer patients would save more lives than the cure of all patients with lip cancer. Small improvement in total survivals in a disease so prevalent means the saving of many lives.

SUMMARY

1. A review of the records of all patients operated on at The Portland Clinic for gastric ulcer and gastric cancer during a 6 year period (January 1946 to January 1952) confirms the fact that in a high percentage of cases benign and malignant ulcers are indistinguishable either preoperatively or at operation.

2. This results in completely inadequate operations in those patients proving to have malignant lesions.

3. To circumvent this possibility radical subtotal gastrectomy is advocated for all gastric ulcers. There has been no increase in operative mortality resulting from such extension of simple ulcer resections.

4. Radical gastrectomy, total and subtotal, has been re-emphasized and a plea has been made for more general standardization and wider use of these procedures.

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BONE CHANGES FOLLOWING BILATERAL URETEROSIGMOIDOSTOMY

MARY S. SHERMAN, M.D., F.A.C.S., New Orleans, Louisiana

THE OPERATION of transplantation of the ureters to the bowel was first devised for the treatment of exstrophy of the bladder. The most popular technique, devised by Maydl in 1894, involved the use of that portion of the bladder wall which contains the ureteral orifices. In order to extend this type of surgery to those cases in which total cystectomy was necessary, direct transplantation of the ureters to the bowel was tried. However, the immediate and delayed mortality from this procedure was so enormous that by 1909, according to Steinke, there were only 35 cases recorded in the literature. Most surgeons preferred the safer but aesthetically less acceptable operation of cutaneous transplantation.

In the succeeding two decades, largely through the work of Coffey (1, 2), significant advances in surgical technique greatly reduced the hazards of ureterosigmoidostomy. With the introduction of antibiotic therapy, this type of surgery became applicable not only in the radical treatment of malignant disease but also in the management of nonmalignant conditions such as vesicovaginal fistula and Hunner's ulcer. In the last 20 years, therefore, there has been a small but steadily increasing group of patients who have survived by long periods the operation of bilateral ureterosigmoidostomy.

Even with optimum conditions the incidence of retrograde infection, ultimately compounded by the development of stenosis about the artificially created orifice, was distressingly high. The resultant kidney damage explained the frequent occurrence of acidosis which when it became troublesome was treated systematically by the administration of sodium bicarbonate. It was even noted by Pines that such a state could lead to bone changes. Because of the emphasis on the role of kidney damage, little attention was paid to this phenomenon of acidosis until relatively recently.

Clues were supplied by Jewett (5, 6) but they were not pursued until Ferris and Odel began to wonder about the electrolyte pattern of the blood in their patients with bilateral ureterosigmoidostomy. They found an absolute increase in the plasma chloride, with a reduction in the bicarbonate, in the presence of a normal or elevated blood urea, but a normal value for creatinine. Furthermore, they had the opportunity to study in detail 3 patients in whom there existed an undoubted state of hyperchloremic acidosis. The first patient was relieved of symptoms and electrolyte imbalance by 5 days of rectal lavage with tap water. It was this experience which suggested the possibility of acidosis due to chloride resorption by the sigmoid. The second patient maintained a normal blood electrolyte pattern as long as he had rectal incontinence. With the development of control he also developed hyperchloremic acidosis. The third patient had had his bilateral transplant for 9 years before he was hospitalized with hyperchloremic acidosis. His condition necessitated a unilateral nephrolithotomy at which time normal excretion of chloride was demonstrated.

On the basis of this telling evidence, Ferris and Odel concluded that a certain number of patients, who had had bilateral ureteral transplants to the bowel and who had developed good bowel control, developed also hyperchloremic acidosis because of chloride absorption by the rectosigmoid in the presence of normal kidney function. They concluded further that in those patients who develop such acidosis early in their postoperative period the amount of sodium chloride poured into the body is probably at fault. In those patients who develop the hyperchloremia late, the syndrome depends either upon the amount of in-

From the Department of Surgery, Division of Orthopedic Surgery, University of Chicago.

Presented in the Forum on Fundamental Surgical Problems before the Clinical Congress of the American College of Surgeons, New York, September 22 to 26, 1952.

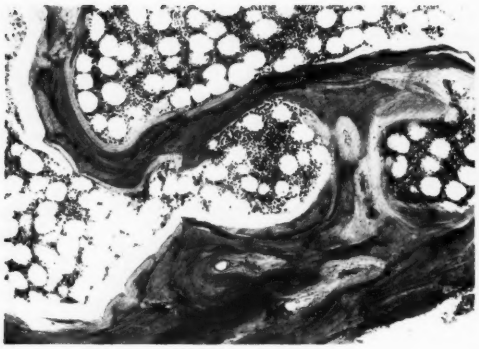

Fig. 1.

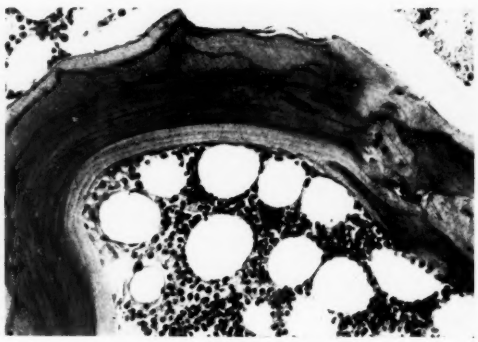

Fig. 2.

Fig. 1. Photomicrograph, ×55. All surfaces are outlined by wide seams of light-staining osteoid tissue which stands in sharp contrast to the bone. The marrow is perfectly normal and shows none of the fibrosis which would indicate secondary hyperparathyroidism.

Fig. 2. Same, ×155.

gested sodium chloride or upon increasing absorption from the rectosigmoid as the patient's ability to retain urine for longer and longer periods increases. The exact mechanism of this selective resorption is not yet clear and furthermore it is noted that the time of development of the syndrome differs from patient to patient.

Further study of a group of 141 patients with bilateral ureterosigmoidostomy revealed that 79 per cent developed some degree of hyperchloremia, usually within a year after the surgery (4). Eighty per cent of the same patients exhibited a decrease in the carbon dioxide combining power of the plasma. In most cases these altered laboratory findings were not accompanied by clinical symptoms of acidosis.

It is obvious that the body's normally operating buffer systems could not be expected to cope with an acidosis of this type. One might expect, therefore, that the bones, with their great reservoir of easily available base, would suffer. When this occurs and the lowered serum calcium is bolstered by calcium derived from the bones, the stage is set for the development of osteomalacia (9). Whether or not osteomalacia will become established evidently depends upon the severity of the electrolyte imbalance and the faithfulness with which it is combatted.

Four patients observed in the light of this theory are of particular interest:

CASE 1. S.Z., a 57 year old woman, had bilateral transplants for carcinoma of the bladder. She was rather well during the succeeding 9 months, when she died suddenly of a cerebral metastasis. There were never any symptoms or findings of significant acidosis except terminally. As might be expected, the sections of the bones were quite normal.

CASE 2. J.P., a 3 year old boy, suffered multiple severe injuries when he was run over by a truck. Because of his precarious condition it was not possible to effect a primary repair of his ruptured urethra. Sufficient atrophy of the bladder resulted so that ureteral transplants were necessary. These have functioned satisfactorily although the patient never developed good rectal control. Since his operation he has had varying degrees of acidosis, but each attack has been treated promptly and effectively with sodium bicarbonate. At no time have his roentgenograms demonstrated any changes suggestive of rickets. Bone biopsy performed 3 years after his transplants, at a time when he had had no symptoms for many months, revealed normal structure.

CASE 3. I.M., a 34 year old woman, had bilateral ureteral transplants performed because of a recurrent vesicovaginal fistula. She had fairly constant acidosis which was incompletely controlled by sodium bicarbonate. Four years after her operation she began to have pain in the neck, back, chest, and ankles. She found it hard to pick things up from the floor and quite difficult to get up from a chair. Roentgenograms made at this time, when her carbon dioxide level was 16.8 millimols per liter, showed a generalized decrease in density. The significance of these findings, which almost certainly indicated osteomalacia, was not appreciated. The patient was given symptomatic therapy and was lost from observation.

CASE 4. P.S., a 26 year old nurse, had bilateral ureteral transplants for relief from a Hunner's ulcer. Five years later she had a nephrectomy because of acute pyelitis. Six years after her transplants, the

patient began to have thoracic pain which appeared with activity and was relieved by rest. This grew steadily worse, and 6 months later the patient was unable to get out of bed. She remained bedridden for 3 months and was then able to get about with the same sort of pain she had had in the beginning. During this time her nonprotein nitrogen remained relatively normal. On the only occasion on which they were investigated (shortly before her skeletal symptoms appeared) the serum carbon dioxide was 16.8 millimols per liter, the serum hydrogen ion concentration 7.39, and the serum chlorides 111 milliequivalents per liter.

One year after her bone pain began the patient was hospitalized for investigation. The chief findings were a marked thoracic kyphosis and severe atrophy of all of the bones of which roentgenograms were taken. Joint changes were minimal. Complete chemical studies were not performed, but the serum chloride at this admission is recorded as 121 milliequivalents per liter. The clinical diagnosis of osteomalacia was sustained by the iliac biopsy which revealed florid changes. Everywhere the surfaces of the old trabeculae were covered by wide osteoid seams (Figs. 1 and 2). It is of interest that the marrow shows no traces of secondary hyperparathyroid activity.

The disorder in this patient should respond rapidly to alkali therapy.

SUMMARY

As so often happens, surgical advance has brought its own new complications, but fortunately these are controllable. It seems evident that when a patient undergoes a successful bilateral ureterosigmoidostomy he is in constant danger of hyperchloremic acidosis even when his kidney function is normal. If such acidosis continues untreated, the development of osteomalacia is a real hazard. Preventing this complication by control of the electrolyte balance depends upon frequent emptying of the sigmoid, reduction of chloride intake, and increase in ingested base.

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ELECTROLYTE CHANGES IN HEALING MUSCLE WOUNDS IN THE DOG

J. A. SCHILLING, M.D., F.A.C.S., A. B. McCOORD, Ph.D., S. W. CLAUSEN, M.D., T. J. WHELAN, JR., M.D., and S. J. KUYKENDALL, M.D., Rochester, New York

THE purpose of this experiment was to determine changes in tissue electrolyte patterns in healing wounds, and to determine the effect of the administration of large amounts of sodium chloride and ACTH on these electrolyte patterns. There have been many studies, particularly recently, on the metabolic response of patients to trauma and surgery, with much attention given to the stress reaction and the administration of ACTH. Sodium retention may occur under these circumstances with considerable potential influence on the electrolytes inside and outside the cells involved in the healing of the local wound. However, our findings revealed rather constant changes in the electrolyte patterns in healing muscle wounds in dogs with no significant influence of large amounts of sodium chloride or ACTH. Administration of ACTH did cause significant transitory changes in normal muscle electrolyte patterns. At the site of the wound, sodium is rather constantly increased and potassium is decreased. Infection markedly exaggerates these local changes, which tended to return to normal ranges at 7 to 8 days after wounding.

METHOD

Healthy, gentle, mongrel dogs weighing 15 to 20 kilograms were selected for these experiments after a period of observation in the animal house. The animals were then placed in metabolism cages and given a standard diet of horse meat and low protein mixture described in earlier publications (6, 7). Six wounds were placed on the abdomen of the animals as depicted in Figure 1. The wounds were made sharply with meticulous hemostasis and reapproximation with 0000 silk sutures, intravenous nembutal anesthesia being used. Normal muscle and blood were secured for control electrolyte determinations. After 6 hours the first biopsy was taken through the area of the abdominal muscle wound and a control biopsy of distant normal muscle was again secured from the rump or shoulder. These and subsequent wound and control biopsies were carried out with subdermal injection of novocain when needed, with care to avoid infiltration of the wound site. Considerable care was given to gentle handling of the muscle tissue as it was removed, as rough handling or squeezing will cause a 25 to 40 per cent variation in electrolyte values and therefore is an important variable in all muscle analyses. Winfield has previously described the decreases in potassium in direct relation to the amount of tissue injury.

The muscle tissue was then divided into two parts and weighed to within 0.5 milligram. The chlorides were determined on one portion after the method of Van Slyke. The other portion was used for potassium and sodium determinations, after drying to a constant weight at 100 degrees C., extraction of fat with an ethyl-alcohol-ether mixture and a chloroform-methyl-alcohol mixture, and ashing in a muffle furnace at 410 degrees C. A flame photometer, utilizing lithium as an internal standard, was used for the electrolyte determinations. All urines were collected and analyzed for electrolyte content to enable sodium, potassium, and chloride balances during the study period, which lasted 7 days after the initial wounding. Subsequent biopsies were secured from the wounds at 1, 1½, 2, 3, 4, and 7 days. One group of 6 animals were maintained on the standard diet only. Another group of 4 animals received 10 grams of sodium chloride daily in their diet during the period of study after wounding. A third

From the Departments of Surgery and Pediatrics of the University of Rochester School of Medicine and Dentistry, Rochester, New York. This study was assisted by a grant from the Office of Naval Research.

group of 4 animals received 50 milligrams of ACTH twice a day intramuscularly and 10 grams of sodium chloride orally each day. Another group of animals received the same amount of sodium chloride intravenously. Total water volumes of muscle tissue were determined by subtracting the dry from the wet weight. The extracellular water volume was calculated on the assumption that all chlorides were extracellular using a Donnan equilibrium factor of 0.95 and a serum protein dilution factor of 0.93. This method is subject to the criticism that there is a small fraction of chloride intracellularly which may be increased with edema, trauma, and inflammatory reaction.

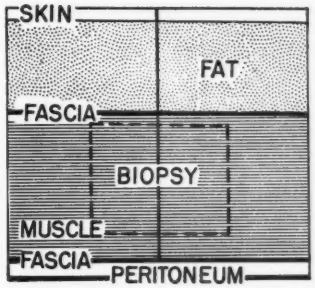

Fig. 1. Location of wounds and site of subsequent biopsies. Normal muscle was secured simultaneously from widely separated areas on the rump and shoulder.

RESULTS

In the control animals the electrolyte changes were remarkably constant in the wounded muscle area (Figs. 2, 3). Early transient changes in the control muscle were consistent with the stress reaction of the initial operative procedure and anesthesia. There was a prompt increase in the total sodium. This was contained in both the extracellular and intracellular fluid compartments as calculated by the extracellular chlorides. The extracellular fluid contained 60 to 75 per cent of this local increase in sodium, the remainder being in the intracellular fluid. There was a 75 per cent decrease in the total potassium in the wounded area, all of which came from within the cell. The chlorides increased in the same range as the sodium values. Phosphorous determinations were complicated by unforeseen technical difficulties and are not included, but they seemed to vary in the same direction as the potassium. For simplicity, anion variations are not included in the graphs. There was a slight increase in total water or wetness in the wounded muscle area which was quite constant. The extracellular water increased in the same range as the increase in sodium and chloride at the expense of the intracellular water where sodium was increased and the remaining potassium was concentrated, thus assisting in maintaining osmotic equilibrium. Infection, when it occurred (Fig. 5), markedly exaggerated these changes in electrolyte patterns in the wounded

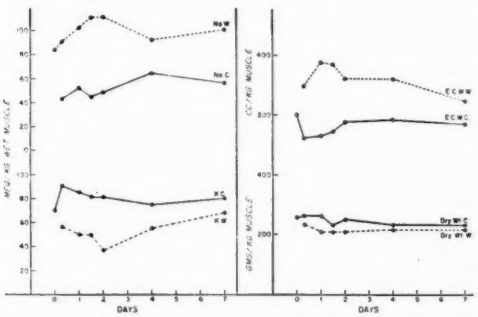

Fig. 2. Control animal (dog 7) on standard diet showing increases in sodium and water and decreases in potassium in the wound (*W*) compared with the normal control muscle (*C*). The decrease in dry weight indicating an increase in total water was much less than the relative increase in extracellular water (*E.C.W.*).

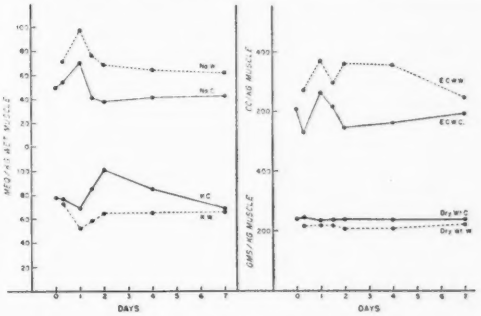

Fig. 3. Control animal (dog 8) on a standard diet with changes in electrolyte and water patterns similar to Figure 2 in the wounded area. The normal control muscle reflects moderately similar changes that are transitory and thought to represent a response to the stress of the operative procedure and anesthesia.

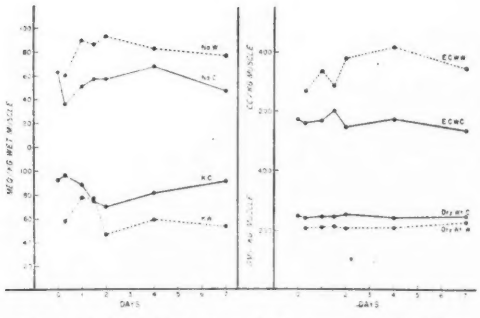

Fig. 4. Animal (dog 9) received 10 grams of sodium chloride a day with no significant differences from control animals in Figures 2 and 3.

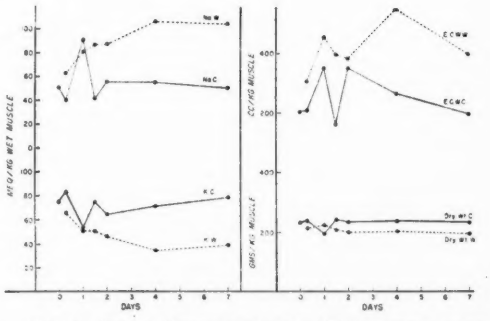

Fig. 6. Animal (dog 11) received ACTH (50 mgm. twice a day) and sodium chloride (10 grams a day) with no significant effect on the previously noted electrolyte changes in the wound area. However, there is marked transient accentuation of the stress response in the normal control muscle tissue associated with an increased loss of potassium in urine and retention of sodium and water.

muscle area. The rather pronounced immediate transitory increases of sodium and decreases of potassium in the normal control muscle tissue seemed to reflect the stress response of the operative procedure and anesthesia and were exaggerated in subsequent animals by the administration of ACTH.

In animals 9 and 10 (Figs. 4, 5) from the group receiving 10 grams of sodium chloride no significant variations from the control animals were noted, except for the influence of infection in Figure 5 just mentioned. Balance studies show a transient retention of sodium the first day followed by a marked saluresis covering the increased sodium intake during the subsequent days.

In animals 11 and 12 (Figs. 6, 7) representative of the group receiving 50 milligrams of ACTH twice a day and 10 grams of sodium chloride daily, no significant variations from the control animals occurred when considering the wounded muscle area. ACTH and sodium chloride exaggerated changes in the electrolyte pattern noted earlier in the control normal muscle tissue secured from distant areas on the rump or shoulder. Sodium increased to values equal to or greater than the wounds themselves. Potassium decreased in amounts equal to or greater than in the wounded area. There was also a significant retention of sodium and water with an increase in wetness of the normal muscle tissue. These changes were transient and were followed by a diuresis and re-

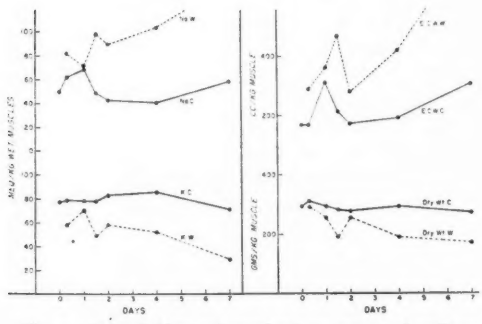

Fig. 5. Animal (dog 10) received 10 grams of sodium chloride a day and developed wound infections with marked accentuation and prolongation of changes in the electrolyte patterns in the wound area, recorded in preceding graphs.

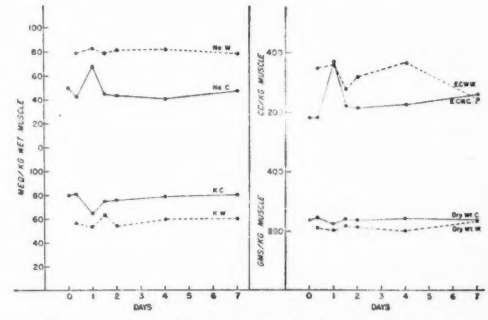

Fig. 7. Animal (dog 12) received ACTH (50 mgm. twice a day) and sodium chloride (10 grams a day) with essentially the same patterns as in Figure 6. In normal muscle the increase in sodium and extracellular water is greater in this instance than loss of potassium.

version to values similar in all groups of animals. These changes in the normal muscle seem particularly important as they are representative of a large tissue mass when compared with the local wounds themselves, and therefore of much more importance therapeutically.

DISCUSSION

Several investigators have demonstrated an increase of sodium and a decrease of potassium in injured tissue. Where the area of injury has been large, there have been compensatory decreases of sodium and increases of potassium in the uninjured tissue. Fox was able to demonstrate these changes very nicely in rats with crushed or burned legs using radioactive sodium. Earlier mention has been made of the observations and reviews of Moore and his associates concerning whole body electrolyte changes following surgery which seem to be governed, in part at least, by adrenal activity. It seems of particular interest to us, however, that the local electrolyte changes in healing muscle wounds are uninfluenced by administration of ACTH and/or sodium chloride, indicating considerable autonomy of the wound in its healing process. Obviously when the area of the wound is large these local changes assume considerable therapeutic significance, as in a burn or crushing injury. Yet these changes are relatively constant and reversible and seem to be much less in total magnitude than those relating to the whole body and its stress response. As infection markedly exaggerates the increase of sodium and the decrease of potassium in wounded tissue as well as being a potent destructor of young fibroblasts (4), it should also be considered in planning electrolyte therapy.

Winfield concludes that most of the potassium loss following surgery is from traumatized tissue. Our studies carried out through the first week of the healing cycle indicate that unless the area of injury is large, just the reverse is true: namely, most of the potassium lost comes from normal tissue under the influence of increased adrenal cortical activity. Under these experimental conditions this loss was transitory and easily compensated for, but in the critically ill surgical patient this reaction is prolonged and must be considered in therapy, particularly when a positive nitrogen balance is achieved. Cannon has very nicely shown that protein repletion in rats is delayed with potassium deficiency. We have observed (5) that potassium is not retained when administered to an animal in negative nitrogen balance. These observations seem important to us in attempting to relate the local response to injury with the whole body metabolic state.

The increase in sodium content of the wound may act as a physical constant, influencing the deposition of collagen by the fibroblast. Vanamee and Porter have demonstrated in tissue culture, utilizing the electron microscope, that collagen may be reconstituted after dissolution by an increase in p_H or by the addition of sodium chloride in concentrations in the same order as those noted in the healing wound in vivo. It seems fair to assume that the proliferating fibroblasts in the wound area undergo the same changes and influences that the surrounding muscle mass does.

SUMMARY

1. Sodium, chloride, potassium, and water concentrations were determined in muscle wounds in dogs during the healing process. These values were compared with normal muscle removed simultaneously during the same period.

2. Sodium and chloride increased promptly and potassium decreased in the region of the healing wound. These changes were markedly exaggerated and prolonged by infection.

3. There was an increase in extracellular water content with a decrease in intracellular water. Total water content was increased moderately.

4. In normal muscle there was a variable transitory increase in sodium, chloride, and water with a decrease in potassium in most animals during the first 2 days. These changes were exaggerated but not prolonged by ACTH.

5. The administration of large amounts of ACTH and/or sodium chloride orally or parenterally had no significant influence on the changes in the electrolyte pattern of the healing wounds.

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ACUTE CHOLECYSTITIS FOLLOWING OPERATION FOR UNRELATED DISEASE

CLETUS W. SCHWEGMAN, M.D., and WILLIAM E. DE MUTH, JR., M.D.,
Philadelphia, Pennsylvania

ACUTE cholecystitis developing in the early postoperative period following surgical treatment of disease unrelated to the biliary system occurs more commonly than might be appreciated from a review of the surgical literature. Glenn in 1947 reported 17 cases personally observed over a period of 14 years. Sparkman in 1952 reported 5 proved cases of acute cholecystitis which developed in the early postoperative period. Available information obtained from the reports of Sparkman and Glenn is tabulated in Table I. Between January 1, 1930 and January 1, 1953, 17 cases were observed in the Hospital of the University of Pennsylvania.

ANALYSIS OF CASES

Age. The age of our patients ranged from 40 to 78 years (Table II), the average being 59 years. Twelve were males and 5 were females. In 3 of our 17 patients a history of previous symptoms suggestive of gallbladder disease was recorded. At the initial operations the abdomen was opened in 10 patients and gallbladder disease was not detected in any.

Time relationships. The interval between operation and the onset of symptoms varied between 1 and 22 days. In general the duration of the oral fasting period seemed to be of little significance. When, however, the interval between the ingestion of food, liquid or solid, and the onset of symptoms is considered, there seems to be a significant relationship. In 11 (64 per cent) of our patients the onset of symptoms occurred within 48 hours of the ingestion of food. In 3 no food had been taken prior to the onset of symptoms. As nearly as could be determined 4 of Glenn's patients experienced the onset of symptoms in the first day following food ingestion.

Sedation. All of our patients received either morphine, demerol, pantopon, codeine, dilaudid, or combinations of these drugs. Glenn's patients also had received morphine.

Diagnosis. Three of our patients died; the acute gallbladder disease became known at the time of autopsy. Two of the 3 were desperately ill of disease unrelated to the biliary system, and the third developed an obstruction of the ileum secondary to a pericholecystic abscess. This patient's death was directly attributable to the gallbladder disease. In 1 instance (WD) laparotomy was performed after a delay of 14 days. The responsible surgeon suspected a subhepatic abscess. At operation he encountered an acutely inflamed stone-containing gallbladder. In our remaining cases the delay in diagnosis was 3 days or less.

Treatment. Cholecystostomy was performed in 12 of our group of 17 patients. Cholecystectomy was performed in 1 instance and 4 patients were treated without operation.

Pathology. The gallbladder had perforated in 4 of our patients, localized gangrene without perforation occurred in another 4, and a simple acutely inflamed gallbladder was found in 9. In 6 (35 per cent) of our patients no calculi were found. It may be noteworthy that perforation of the gallbladder did not occur in the absence of stones. It is possible, and indeed likely, that in some of these patients stones were present which were not detected at the time of operation. Perforation did not occur in any of our patients under 50 years of age.

Genesis. The response of the gallbladder and extra hepatic biliary systems to natural and unphysiologic stimuli has been studied extensively. Some are obviously not concerned with the development of acute obstruction and inflammation of the gallbladder in the postoperative period. Others may con-

From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania and the Surgical Service of the Hospital of the University of Pennsylvania, Philadelphia.

TABLE I.

Sex	Age, yrs.	Previous operation	Postop. day developed symptoms	Duration of fast, days	Interval food to onset symptoms, days	Sedation	Delay in diagnosis, days	Treatment	Survival	Was disease recognized at 1st operation	Pathologic findings	Previous symptoms	Stones
						Sparkman Cases							
F	58	Repair incisional hernia	4	4	<1	?	0	Cholecystostomy	Yes	?	Acute G.B. with stones & C.D. stones	Yes	Yes
M	49	Ventriculogram	1	?	?	?	6	Cholecystostomy	Yes	No	Gangrene of G.B.	?	?
F	72	Hysterectomy perineal repair	18+	?	?	?	?	Cholecystostomy	Yes	?	Gangrene of G.B.	?	?
M	75	Radium implantation bladder and ureteral meatotomy	8	?	?	?	5	Cholecystostomy	Yes	?	Acute cholecystitis	?	?
M	62	Hip pinning	21	?	?	?	12	Cholecystostomy, drainage abscess	Yes	No	Ruptured G B., pericholecystic abscess	?	?
						Glenn Cases							
M	67	I & D abscess of leg	2	?	?	Morphine, codeine	0	Cholecystostomy	Yes	No	Acute cholecystitis	No	No
M	32	Appendectomy (ruptured)	10	9	1	Morphine	?	Cholecystectomy	Yes	No	Acute cholecystitis	No	No
M	62	Repair inguinal hernia	3	2	1	Morphine, codeine	0	Refused op. 4 mos. later cholecystectomy	Yes	No	Chronic G.B. (4 mos. later)	Yes	Yes
M	41	Nasal packing for epistaxis	5	4	1	Morphine	0	Cholecystostomy	Yes	No	Gangrenous G.B. with perforation		?
M	64	Suprapubic prostatectomy	8	7	1	Morphine	0	Cholecystostomy	Yes	No	Acute cholecystitis		Yes

tribute to the onset of the acutely inflamed gallbladder.

The resumption of oral feedings after a period of fasting. It will be noted that the majority (11 of 17) of the patients reported by the authors manifested signs and symptoms of acute cholecystitis within a day or two after the resumption of oral feeding. Glenn made a similar observation and attributed the onset of the difficulty to the forceful contractions of the gallbladder in response to the ingestion of food after a period of bile stagnation and cholecystic inertia. The kinetic effect of oral feedings, especially certain forms of fat, on the gallbladder and ductal system is well documented. Copher and Illingworth demonstrated that the gallbladder failed to empty for 3 days or more if food was not taken by mouth. The concentration of bile within the gallbladder increases its viscidity and the mucinous material secreted by the gallbladder mucosa adds to its viscosity. Subsequent to the trauma of operation the volume of intestinal fluid, including bile, which can be aspirated with an indwelling intestinal tube is reduced in the immediate postoperative period.

The flow of fresh liver bile is diminished during anesthesia. Graham (5) has suggested that the gradual washing out of the gallbladder by an ingress of fresh liver bile may be an important factor in the mechanism of gallbladder evacuation. Although Newcomer and Newcomer have suggested that a filled stomach and duodenal cap may, by displacement of the liver and gallbladder, straighten the cystic duct and thereby facilitate emptying of the gallbladder, it is clearly evident that gallbladder evacuation does not depend upon gastrointestinal continuity. Cholecystokinin is elaborated and exerts its influence on the gallbladder even if all food by-passes the duodenum. In all probability the renewed contractions of the stagnant gallbladder, induced by the resumption of oral feedings, are a contributing factor in the impaction of

TABLE II.—AUTHORS' CASES

Initials, Hosp. No., Sex	Age, yrs.	Previous operation	Postop. day developed symptoms	Duration of fast, days	Interval food to onset symptoms, days	Sedation	Delay in diagnosis, days	Treatment	Survival	Was disease recognized at 1st operation	Pathologic findings	Previous symptoms	Stones
WL 29063 M	78	Ca sigmoid with obst.—Ileostomy —5/22. Cecostomy—5/14	?	?	No food taken	Morphine, codeine	?	Postmortem finding	No	No	Ruptured acute G.B., pericholecystic abscess	?	Yes
JD 50976 M	67	TUR for Ca prostate	6	6	2	Morphine, demerol, codeine	0	Cholecystostomy	Yes	No	Acute cholecystitis	No	Yes
JH 40701 M	54	Jejunojejunost. for obst. due to regional enteritis	?	?	No food taken	Dilaudid	?	Postmortem finding	No	No	Gangrenous G.B.	No	Yes
JS 73791 M	40	Cup arthroplasty for arthritic hip	1	2	No food taken	Morphine, demerol	0	Cholecystostomy	Yes	No	Acute cholecystitis	No	No
HB 70368 F	67	Midthigh amputation, gangrene foot (diabetes)	2	1	1	Morphine, dilaudid, codeine	2	Cholecystostomy	Yes	No	Gangrenous G.B.	No	Yes
MS 83242 F	48	Transverse colostomy, Ca descending colon with obst.	6	8	1	Demerol, codeine	1	Cholecystectomy	Yes	No	Acute cholecystitis	No	Yes
SH 27271 M	43	Appendectomy 7/14 Ileostomy for obst. 7/22	3	1	2	Morphine, pantopon, dilaudid	3	Postmortem finding	No	No	Acute cholecystitis	Yes	Yes
WD 92432 M	57	Subtotal gastrect. for Ca of stomach	4	5	<1	Morphine, demerol, codeine	14	Cholecystostomy	Yes	No	Acute cholecystitis	No	Yes
CP 90321 M	68	Abdominoperineal resect., Ca rectum	22	17	5	Morphine, demerol, dilaudid	2	Cholecystostomy	Yes	No	Acute gangrenous cholecystitis	No	No
TB 98818 M	65	Left colectomy Ca sigmoid	9	5	4	Demerol, codeine	2	Cholecystostomy	Yes	No	Acute cholecystitis	No	No
WG 98232 M	43	Total gastrect. Ca stomach	11	10	1	Dilaudid, demerol, morphine, codeine	2	Cholecystostomy	Yes	No	Acute cholecystitis	Yes	No
SM 25434 F	65	Retinal electrocoagulation, retinal detach.	7	6½	<1	None	0	Cholecystostomy	Yes	No	Gangrene G.B. with perforation	No	Yes
LR 94251 M	64	Splenectomy, hemolytic anemia	9	5	4	Morphine, codeine	0	Cholecystostomy	Yes	No.	Gangrenous cholecystitis	No	No
AR 98823 F	73	Thyroidectomy for nontoxic goiter. Mastectomy 10 days before	3	2½	<1	Demerol, codeine	0	Conservative. No operation	Yes	Not op. on	Jaundice, tender RUQ mass, leucocytosis, fever	No	Yes
PR 61041 M	65	Ca descending colon, Rankin resection, closure colostomy	5	6	<1	Morphine	0	Cholecystostomy	Yes	No	Gangrene G B. with perforation	Yes	?
MG 55843 F	51	Cystocele perineal repair	3	2½	<1	Dilaudid, codeine	3	Cholecystostomy	Yes	No	Acute G.B. with perforation	No	Yes
JR 37153 M	55	Bronchopleural fistula. Biopsy pleural sinus	2	1½	<1	Pantopon, morphine	0	Cholecystostomy	Yes	No	Acute cholecystitis	No	No

stones or viscid bile into the ampulla of Vater or cystic duct with subsequent acute inflammation.

Drug influence. Many drugs influence gallbladder behavior. Only a few therapeutically employed will be discussed. Walters and associates have clearly demonstrated the effect of morphine upon the dynamics of the common duct. Ten milligrams of morphine produces a rise from the resting state of 0 to 20 millimeters of water pressure to a level of 200 to 300 millimeters. This rise in pressure is measurable within 5 minutes after intramuscular injection, reaches its peak in 15 minutes, and exerts its effect for at least 2 hours. Codeine (64 mgm.), pantopon (20 mgm.), and dilaudid (2 mgm.) all cause a similar but less marked rise of intrabiliary pressure. Gaensler and associates demonstrated that contrary to common belief demerol exerts a spasmogenic rather than a spasmolytic effect on the sphincter mechanism at the lower end of the commun duct. Morphine exerts an inhibitory effect on the gallbladder and causes a contraction of the sphincter mechanism of the common duct. The inhibition of the gallbladder and the constriction of the sphincter mechanism of the lower common duct by morphine supplement the stagnating effect of the enforced fast.

Atropine and scopolamine exert an antispamodic effect on the sphincter mechanism of the common duct but are incapable of overcoming the influence of morphine. These drugs in all probability fail to play any significant role in the etiology of acute cholecystitis.

Kozoll and Necheles were unable to elicit any constant change in intracystic pressures following the intravenous administration of physiologic saline solution but did observe marked spasm of the sphincter of Oddi and duodenum. The intravenous administration of mixtures of 5 per cent glucose and 0.9 per cent sodium chloride solutions produced a slight contraction of the gallbladder and a depression of sphincter and duodenal tone. It is unlikely that the intravenous solutions commonly employed in the postoperative period exert any significant effect on the biliary system.

Miscellaneous factors. It is conceivable that other less tangible factors, not heretofore included, may influence the dynamics of the gallbladder and associated ducts. Whitaker demonstrated that even after bilateral vagotomy the gallbladder emptied in a normal fashion. Howard has shown experimentally in animals that the development of acute cholecystitis may be prevented by sympathectomy.

Changes in intra-abdominal pressure associated with respiration seem to be unimportant in the mechanism of gallbladder evacuation. The position of the patient apparently does not affect cholecystic evacuation as it occurs just as effectively whether the subject is standing or lying. Bockus states that fright, pain, or anxiety states are frequently associated with a temporary cessation of bile flow which might result in biliary stagnation.

DIAGNOSIS

The diagnosis of acute cholecystitis can usually be made without difficulty if it is kept in mind as a possibility. The disease is characterized by pain in the epigastrium and right upper abdominal quadrant. The presence of biliary colic associated with severe pain in the right upper quadrant suggests cystic duct obstruction. The pain, frequently associated with nausea and vomiting, is aggravated by diaphragmatic motion. Upper abdominal tenderness and muscle spasm are the result of peritoneal irritation. In uncomplicated cases the temperature rarely exceeds 102 degrees F. Leucocytosis of moderate degree is expected. Jaundice is not common and if present indicates common duct obstruction. A mass is sometimes palpable in the right upper quadrant.

Acute cholecystitis which develops in the wake of a major operation unrelated to the biliary system may, however, go unrecognized for some time. Abdominal pain, nausea, vomiting, and fever are commonly observed in the postoperative period and are accepted by the surgeon as side effects of the operative procedure. Right upper quadrant pain and tenderness following subtotal gastrectomy direct the attention of the surgeon toward the duodenal stump. Pain in the epigastrium and right

subcostal area may be accepted as symptoms of a subdiaphragmatic collection or an infarct in the right lower lobe of the lung. A palpable tender mass in the right upper quadrant may represent an intra-abdominal abscess. It is, therefore, understandable that an acutely inflamed gallbladder may escape detection for some time.

Some of the uncertainties of diagnosis might be eliminated if during the course of intra-abdominal operations the gallbladder was more regularly palpated. It is suggested that this be done if the organ is accessible and if such palpation does not add to the risk of operation. Those patients, with complaints suggesting biliary tract disease in whom major elective operations are anticipated, might benefit by a preoperative cholecystogram. In this fashion acute inflammation of the gallbladder, which might develop in the immediate and early postoperative period, may be detected earlier and with less difficulty.

TREATMENT

Acute cholecystitis may be treated: (1) conservatively without operation, (2) by immediate cholecystectomy, or (3) by cholecystostomy. The best interest of the patient will be served if each case is considered individually.

If the attack is mild and associated with minimal pain and tenderness, fever, and leucocytosis, it may be prudent to treat the patient conservatively with gastric suction, starvation, antibiotics, and intravenous fluid. The risk associated with nonsurgical treatment is less in the young than in the patient 50 years of age or older. It is important to remember that peritoneal infection in the aged may be misleading, for the signs of peritoneal irritation and the systemic manifestations of infection may be of a very low order.

For the past 20 years Graham (6) and Zinninger have advocated immediate cholecystectomy in acute cholecystitis. This attitude is acceptable to an ever increasing number of surgeons. If the gallbladder is removed within 48 hours of the onset of the disease the removal is usually simple, safe, and curative.

While cholecystostomy is considered a procedure of compromise it is the operation of choice in patients too ill to withstand cholecystectomy safely and in whom the technical difficulties encountered render the operation hazardous. Cholecystostomy under local anesthesia is usually safe and at least temporarily effective in even the most seriously ill patient. Under ordinary circumstances the previously drained gallbladder should be removed at a later date unless valid contraindications exist.

CONCLUSIONS

The recognition of acute cholecystitis occurring in the postoperative period may be difficult. The symptoms of gallbladder disease are frequently mistaken for the usual postoperative sequelae or other complications. In all probability, in some cases cited in our series, a higher index of suspicion of this complication would have led to earlier diagnosis.

It would appear that the ingestion of food after a period of fasting might precipitate an attack of acute cholecystitis in the postoperative period. The kinetic effect of ingested food on cholecystic contraction may be largely responsible for the chain of events. The effect of narcotics, commonly used postoperatively, on the biliary tree is well documented, and the evidence favors the concept that biliary stagnation may result from the use of these drugs. As previously suggested by Glenn, the forcible contraction of the gallbladder in response to the ingestion of food may be responsible for the onset of acute cholecystitis following prolonged stagnation due to fasting and narcotics.

Three of our patients expired. It is interesting that all were treated without operation. At the time of laparotomy the gallbladder, if accessible, should be palpated if this maneuver will not increase the risk of operation. Since perforation did not occur in any patient under 50 years of age, we believe that acute cholecystitis developing in the postoperative period is a much less serious complication in the young. In our series acute cholecystitis occurred in the male more than twice as frequently as in the female. This unexpected ratio does not correspond to the true incidence of cholecystic disease in the sexes. A gangrenous stone-free gallbladder was found in 2. Perforation did not occur in the absence of stones in the gallbladder. The high incidence

(35 per cent) of calculi-free gallbladders in this series is unexplained.

There is general agreement that acute cholecystitis is nearly always dependent upon obstruction of the cystic duct. In over 90 per cent of cases the offensive agent is an impacted calculus. The absence of stones in the gallbladder at the time of operation or necropsy does not prove that such stones were not present earlier. In about 5 per cent of patients with common duct stones the gallbladder is stone-free. Cystic duct obstruction may be caused by angulation of the duct, by offensive adhesions, an adjacent peptic ulcer, or by extrinsic pressure. Occlusion of the cystic duct may, on occasion, be produced by viscid, inspissated bile. Experimental evidence suggests that an increase in bile salt concentration within the gallbladder is responsible for acute cholecystitis. The severity of the inflammation is proportional to the content and the concentration of the obstructed bile.

Acute cholecystitis developing soon after a major operation is a serious complication. It is understandable in this group of patients that the surgeon often prefers to drain the gallbladder rather than to remove it.

SUMMARY

Data relating to 17 of our own patients and 10 patients previously reported by Glenn and Sparkman who developed acute cholecystitis following operation on unrelated systems are tabulated. The possible relationships of the fast period with subsequent food ingestion and the employment of narcotics in the development of acute cholecystitis in the postoperative period are discussed. In our group of 17 patients gangrene or perforation of the gallbladder was found in 8 (47 per cent). The high incidence of calculi-free gallbladders is unexplained. Treatment is discussed and the pathologic findings are tabulated.

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THE BLOOD VOLUME IN PREGNANCY AS DETERMINED BY P^{32} LABELED RED BLOOD CELLS

NATHANIEL I. BERLIN, Ph.D., CARL GOETSCH, M.D., GRACE M. HYDE, M.D., and ROBERT J. PARSONS, M.D., Berkeley, California

IT has been known for many years that the concentration of red blood cells in the peripheral blood as determined by the red cell count, hemoglobin, or hematocrit decreases during the course of pregnancy. This has been termed the physiologic anemia of pregnancy. The term arose from the fact that early investigators had suspected that this was merely a hydremia and that the total quantity of cells in the circulating blood was normal. Later measurements of the blood volume using the dye methods confirmed these opinions. The studies of the blood volume in pregnancy have been reviewed recently by Caton and co-workers, McLennan and Thouin, and Tysoe and Lowenstein. In general there is agreement that there is a progressive increase in the plasma volume and total blood volume during the course of pregnancy with a maximum in the ninth month. The possibility of a decrease during the ninth month, before delivery, is controversial. As calculated from the plasma volume and hematocrit, most authors agree that there is a progressive increase in the total red cell volume during pregnancy but this is much smaller than that observed for the plasma volume both in terms of absolute values and percentage-wise. There is only one study in the literature, that of Caton and co-workers (3), in which the total volume of red cells was determined directly, by the use of radioiron labeled red cells. This study showed a progressive increase in the total red cell volume during the course of pregnancy. A third observation on blood volume in pregnancy, which has largely escaped attention, has been the decrease or change in blood volume between the immediate antepartum period and the immediate postpartum period. Lowenstein and co-workers found that this amounts to approximately 1,200 cubic centimeters. The figures of Caton and co-workers confirm this. The present paper is to report the studies of the blood volume during the course of pregnancy as determined with P_{32} labeled red blood cells in 181 women.

From the Donner Laboratory of Medical Physics, University of California, Berkeley, and the Pathology Laboratory and Obstetrical Service, Highland-Alameda County Hospital, Oakland, California.

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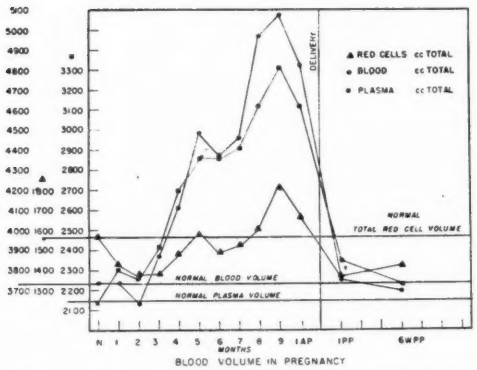
METHODS

The blood volume was determined by the method of Hevesy and Zerahn as modified in this laboratory (2). One hundred and fifty-seven pregnant patients and 34 postpartum patients were studied. Sixty-two patients seen in the first and second trimesters were from the private practice of one of us. The remainder were from the obstetric service of the Highland-Alameda County Hospital. In order to simplify the problem of patient cooperation and more importantly to avoid repeated injections of radioactive materials, only one determination was done on each patient. All patients were followed until delivery and were then grouped according to the interval of time between the determination of the blood volume and the date of delivery. Only patients with a normal pregnancy and delivery were included. All patients were routinely placed on oral iron at the time of their first visit. The blood volume of 16 healthy, nonpregnant women of the child bearing age was used to establish a normal value for the blood volume in women (1).

RESULTS

The results are tabulated in Table I and graphically presented in Figures 1 to 3.

Total red cell volume: Figure 1 and Table I show that there is an initial drop in the total red cell volume of approximately 200 cubic centimeters during the first 2 months


RED CELLS cc TOTAL
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DELIVERY
NORMAL TOTAL RED CELL VOLUME
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NORMAL PLASMA VOLUME
N 1 2 3 4 5 6 7 8 9 IAP IPP 6WPP
MONTHS
BLOOD VOLUME IN PREGNANCY

Fig. 1. The blood volume in pregnancy. IAP, immediately antepartum (0 to 2 days before delivery); IPP, immediately postpartum (0 to 2 days postpartum); 6WPP, 6 weeks postpartum.

reaching a minimum in the second month of pregnancy. This is followed by a progressive rise to a peak in the ninth month, which is 270 cubic centimeters above the normal nonpregnant value. The last month before delivery shows a 170 cubic centimeter decrease in total red cell volume. At delivery and during the immediate postpartum period there is further decrease of 300 cubic centimeters to a level which is approximately 200 cubic centimeters below normal. During the 6 weeks' postpartum period there is a small but probably statistically significant increase but the level obtained is still 140 cubic centimeters below the normal level.

Plasma volume. Beginning with the first month of pregnancy there is a definite but steady increase in the plasma volume which reaches a peak in the ninth month, approximately 1,200 cubic centimeters above the normal value. As with the total red cell volume, there is a significant drop of 190 cubic centimeters prior to delivery. In the immediate postpartum period the plasma volume falls another 780 cubic centimeters, but is still 180 cubic centimeters above the normal value. By the end of 6 weeks postpartum the volume is still 100 cubic centimeters above normal.

Total blood volume. Because the fall in the total red cell volume is greater than the rise in plasma volume in the first 2 months of pregnancy there is a small drop in the whole blood volume during this period. Following this the rapidly increasing plasma volume is reflected in a rapid climb in the total blood volume with a maximum increase averaging 1,400 cubic centimeters. During the last month of pregnancy the total blood volume drops 350 cubic centimeters and immediately after delivery the volume has diminished an additional 1,100 cubic centimeters so the total blood volume immediately postpartum is about the normal level for the nonpregnant woman.

TABLE I.—THE BLOOD VOLUME IN PREGNANCY

Month	No. of cases	Blood volume, c.c.		TRCV, c.c.		Plasma volume, c.c.	
		Total	S.E. of mean	Total	S.E. of mean	Total	S.E. of mean
Normal	16	3726	110	1562	49	2140	69
1	6	3431	261	1422	122	2308	145
2	12	3638	136	1352	49	2259	93
3	15	3865	105	1388	40	2407	91
4	22	4160	123	1443	46	2706	91
5	12	4487	132	1595	60	2778	66
6	14	4355	214	1485	66	2857	152
7	12	4452	220	1518	91	2903	59
8	21	4964	148	1607	65	3120	95
9	15	5177	176	1833	80	3305	114
IAP	18	4820	188	1657	65	3118	147
IPP	17	3745	138	1363	74	2339	76
6WPP	17	3692	209	1421	65	2249	106

TRCV = Total red cell volume.
IAP = Immediately antepartum.
IPP = Immediately postpartum.
6WPP = 6 weeks postpartum.

DISCUSSION

Previous workers have shown a definite increase in circulating total red cell volume, plasma volume, and whole blood volume during normal pregnancy, but no previous study has pointed out, as do the data presented here, that there is an initial drop in the total red cell volume. This indicates that there is a true anemia during the first and second trimesters and that the decrease in red blood count and hemoglobin is not entirely due to hydremia, as has been postulated. The mechanism for the development of this anemia is not known. Since it does not seem possible that this anemia is due to

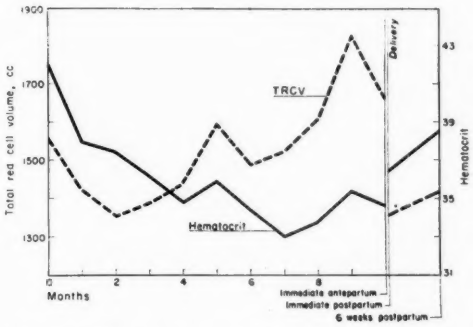

Fig. 2. The total red cell volume and hematocrit in pregnancy.

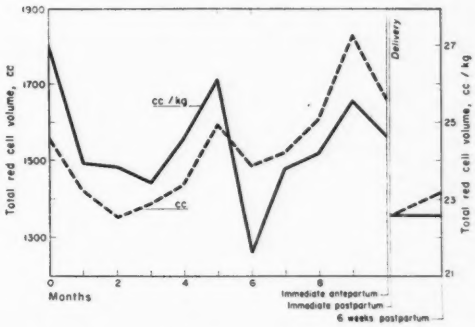

Fig. 3. Comparison of total red cell volume in absolute values and cubic centimeters per kilogram body weight.

external blood loss, it should, therefore, be the result of either a decrease in the rate of formation of red cells or a decrease in the life span of the red cell, or a combination of both factors. It is possible that the endocrine changes occurring during pregnancy may profoundly influence the bone marrow. If it is assumed that this decrease in total red cell volume occurs uniformly during the first 2 months of pregnancy and is due only to a change in the rate of formation of red cells; then, during 42 days, there is a 200 cubic centimeter decrease or approximately 5.0 cubic centimeters per day. In the normal woman approximately 12 cubic centimeters of red cells are produced per day. If then this decrease is due to a decrease in the rate of formation of red cells the pregnant woman would be producing only 7 cubic centimeters per day of red cells or 58 per cent of normal. Studies of iron metabolism with radioactive iron designed to measure the rate of production of red cells would provide the answer to this question. Studies of the life span of the red cell would probably not be satisfactory since, during the time required to measure this, profound changes in both the total red cell volume and over-all metabolism are taking place.

A statistical analysis of the data obtained from the patients during the 0 to 2, and 2 to 28 days antepartum periods indicates that there is a significant decrease in the total blood volume, total red cell volume, and plasma volume during this period. Analysis of the difference between the two means indicates that the probability is less than .001 that this is due to chance. This decrease in blood volume during the last month of pregnancy is, therefore, statistically significant and the finding is in agreement with the work of Thomson and co-workers and Caton and co-workers (4).

The work of Lowenstein and co-workers showing a marked decrease in blood volume at the time of delivery is well confirmed by this study. During the intervals from immediately antepartum to immediately postpartum and 6 weeks postpartum the total blood volume returns promptly to the level of a normal nonpregnant woman and remains there. However, the return to a normal value of the total red cell volume and plasma volume is a slow process. Even at 6 weeks postpartum the total red cell volume is below normal while the plasma volume is elevated. The study of Magee and Milligan, although confined to concentration of red cells in the peripheral blood, indicates that observations for a period of as long as a year after delivery may be necessary in order to observe a return to normal values.

The effect of supplemental dietary iron on our observations is hard to evaluate. The good agreement in values of the total red cell volume in these patients and those studied by Caton and co-workers (3) with radioactive iron-labeled cells who were not given supplemental iron would suggest that there was little or no effect of the supplemental iron on

the total red cell volume in normal pregnancy. Furthermore, the studies of Lund show that in normal pregnant women given supplemental iron the increase in total hemoglobin is only slightly greater, a 23 per cent increase as compared to the 15 per cent increase in the total hemoglobin in controls not given supplemental iron.

Figure 2, showing the total red cell volume and the hematocrit, indicates clearly that during the course of pregnancy there is an early rapid decrease in the hematocrit reaching a minimum in the third trimester followed by a progressive rise in the seventh, eighth, ninth months, and in the antepartum period. Comparison with the total red cell volume shows that the measurement of concentration of red cells in the peripheral blood is grossly inadequate to describe the changes in total red cell volume since during the period when the hematocrit is still continuing to decrease, the total red cell volume is rising, and conversely, while the hematocrit rises there has been noted a marked fall in the total red cell volume, i.e., in the ninth month and between the immediate antepartum and the immediate postpartum period. This clearly indicates, as we have shown for other disease states, that the hematocrit is a grossly inadequate measure of the total volume of red cells.

This type of analysis comparing different groups of individuals taken at different times is subject to certain limitations. It is our opinion that the groups are sufficiently large to be significant, although we realize that they are not as large as they should be absolutely to prevent chance variation in the blood volume from producing the observed findings. However, examination of Figure 3 in which the total red cell volume is plotted both in absolute values and in cubic centimeters per kilogram body weight shows that the values closely parallel each other, indicating that one could use either method for graphically presenting the data. Since there are marked changes in body weight during pregnancy the comparison of blood volume as expressed in cubic centimeters per kilogram of body weight in an analysis of this type is less satisfactory than comparing the absolute values for the blood volume.

SUMMARY

1. The total blood volume has been determined in 181 pregnant or postpartum women.

2. There is a true anemia in the first and second trimesters of pregnancy.

3. Previous observations of a progressive increase in the plasma volume up to the ninth month of pregnancy have been confirmed.

4. At delivery there is a decrease in the blood volume of approximately 1,100 cubic centimeters.

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MULTIPLE ORGAN RESECTION FOR ADVANCED CARCINOMA OF THE COLON AND RECTUM

JOHN VAN PROHASKA, M.D., F.A.C.S., MICHAEL C. GOVOSTIS, M.D., and MILAN WASICK, M.D., F.A.C.S., Chicago, Illinois

CARCINOMA of the colon and rectum is often found at operation in a state of extensive local invasion of adjacent organs and structures. In some instances the local spread renders the lesion obviously and hopelessly inoperable. In others, the malignant lesion, even though it involves more than one organ, may still be contained in its visible entirety within the perimeter of radical resection.

Invasive cancer presents situations in which the surgeon must evaluate the resectability of the lesion in terms of technical feasibility, in terms of hazards presented by the operation, in terms of the estimated duration of survival of the patient, and finally in terms of the anatomic and physiologic defects created by the operation. The analysis of the surgical results obtained in multiple organ resection for advanced carcinoma of the colon and rectum seems to be a desirable criterion upon which the surgeon may predicate his important decisions. Without this analysis the surgeon would be less able to find a proper attitude between wanton radicalism on the one hand and abdicative conservatism on the other.

It is natural to assume that the greater the local involvement, the greater the chances for distant metastases. There is no doubt that this unfortunate relationship between the locally spreading lesion and the distant site of metastases exists in many patients. Yet, the existence of an infiltrating carcinoma cannot always be used as a sign of inoperability. A neoplasm which has left its primary site of origin and established itself in a neighboring organ or structure without visible or palpable distant metastases constitutes the desirable case for multiple organ resection. In the presence of such circumstances the entire lesion may be eradicated in continuity with the primary neoplasm.

The purpose of this paper is to point out that operability of advanced carcinoma of the colon and rectum may be extended by approximately 9 per cent. This type of radicalism should be accomplished without markedly increasing the operative mortality and without inflicting crippling anatomic and physiologic defects upon the patient whose survival time may be limited by the spreading neoplasm.

In a survey of 225 consecutive operations for carcinoma of the colon and rectum, 21 patients were found at operation to have lesions which at first appeared to be inoperable. These lesions had spread from the primary sites to various neighboring structures and organs. The common sites to which these carcinomas had spread either by direct contact or by regional lymphatics were the parietal peritoneum, abdominal wall, fallopian tubes, uterus, urinary bladder, duodenum, pancreas, stomach, spleen, and the diaphragm. These patients were thoroughly explored to rule out distant intra-abdominal metastases, and to determine resectability. Wide exposures were required to facilitate exploratory dissections of the neoplasm. This initial dissection was performed without destroying the blood supply. The operation could be terminated without harming the patient if the exploratory dissection revealed the mass to be inoperable. In all cases, the cohesion between the primary lesion and the adjacent organ and structure was due to carcinomatous infiltration rather than to an inflammatory process alone. This was confirmed, in every instance, by histopathologic examination. The operative excision included the entire neoplastic mass removed en bloc. The resection in continuity, of course, was not possible in cases requiring partial resection of the liver. A survey of the patients on whom radical surgery was performed is presented in Table I.

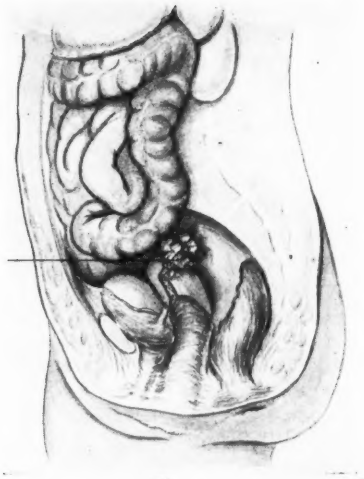


Fig. 1.

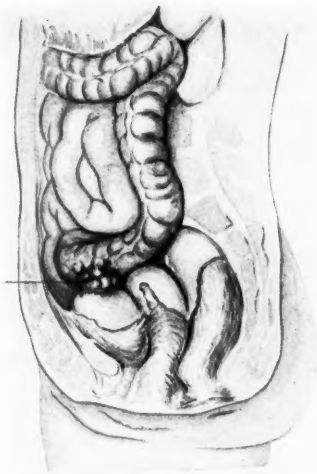


Fig. 2.

Fig. 3.

Fig. 1. Carcinoma of the rectum showing invasion of the body of the uterus. An adequate operation for this type of lesion is a combined abdominoperineal resection in continuity with total hysterectomy and bilateral salpingo-oophorectomy.

Fig. 2. Carcinoma of the rectosigmoid colon showing invasion of the urinary bladder. This is the type of lesion in which one-half of the urinary bladder was removed in continuity with resection of the sigmoid colon.

Fig. 3. Roentgenogram of patient T.G. showing carcinoma of splenic flexure with obstruction to the retrograde flow of barium. In order to encompass this lesion it was necessary to perform partial gastrectomy, partial pancreatectomy, splenectomy, left hemicolectomy, and resection of one-fourth of the left diaphragm.

Fig. 4. Patient T.G. showing the surgical problem (radical left hemicolectomy) and the reconstruction after resection (schematic).

Fig. 5. Patient T.G. before surgery.

Fig. 6. Patient T.G. 3 weeks after radical surgery. The left diaphragm was partially excised and advanced to a higher level on the thoracic cage.

DISCUSSION

The analyses of data presented in Table I indicate that the best results were obtained in patients with primary carcinoma of the rectum infiltrating the body of the uterus. All patients in this series are alive and well. It is interesting to note that the 2 patients who have survived 10 years were treated as inoperable elsewhere.

The patients with an infiltrating neoplastic process into the abdominal wall or perineum had the poorest results. In the 7 cases presented in this series, it was not always possible to ascertain whether the neoplastic extension was caused by infiltration through regional lymphatics or by tissue contact. Only 1 patient survived 5 years.

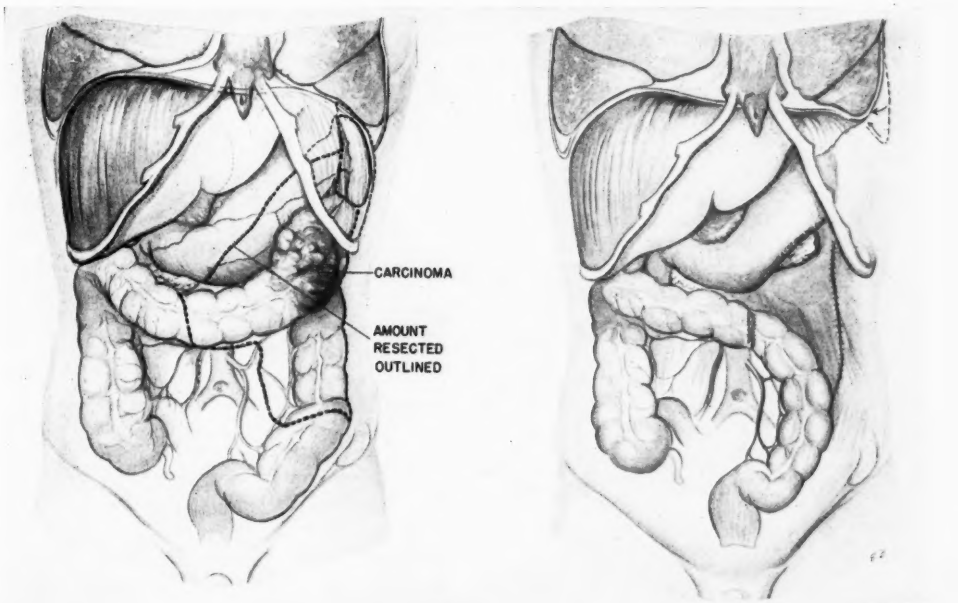


Fig. 4.

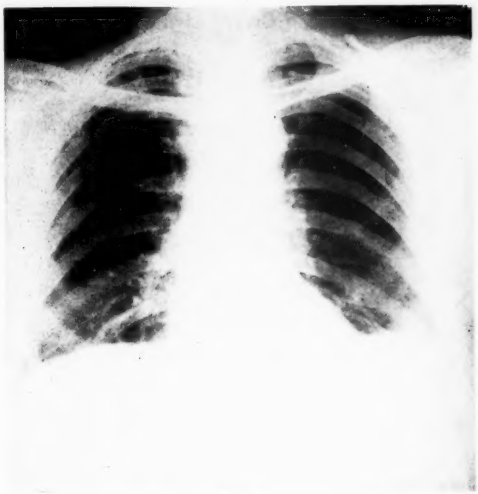


Fig. 5.

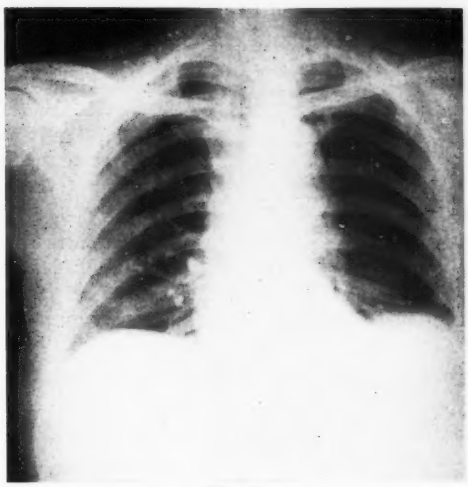


Fig. 6.

(*Legends on opposite page.*)

The patients with carcinomas of the rectosigmoid or sigmoid with contact invasion of the dome of the urinary bladder had satisfactory results. They survived 3 to 4 years without urinary distress. This type of lesion, whenever resectable, should be removed because of the possible development of colovesical fistula.

In the 225 operations performed, only 2 patients had resectable "solitary" liver metas-

TABLE I.—SUMMARY OF RESULTS IN MULTIPLE ORGAN RESECTIONS IN ADVANCED CARCINOMAS OF THE COLON AND RECTUM

Patient	Sex	Age, years	Diagnosis	Operation	Results
A.K.	F	65	Ca. rectum.	Combined abdominoperineal; total hysterectomy; bilateral salpingo-oophorectomy	10 years alive
M.P.	F	64	Ca. rectum	Combined abdominoperineal; total hysterectomy; bilateral salpingo-oophorectomy	10 years alive
M.I.	F	59	Ca. rectum	Combined abdominoperineal; total hysterectomy; bilateral salpingo-oophorectomy	4 months alive
B.C.	F	58	Ca. sigmoid	Resection of sigmoid, one-half of urinary bladder	4 years died of liver metastases
E.B.	M	61	Ca. sigmoid	Resection of sigmoid, one-half of urinary bladder	4 years alive
D.J.	M	66	Ca. sigmoid	Resection of sigmoid, one-half of urinary bladder	3 years died of peritoneal and liver metastases
L.Z.	M	67	Ca. rectum	Combined abdominoperineal; part of perianal area	1 year died of metastases
M.B.	M	56	Ca. rectosigmoid	Combined abdominoperineal; partial resection of abdominal wall	1 year died of metastases
P.P.	M	63	Ca. rectum	Combined abdominoperineal; second stage resection of perianal area	3 years died of metastases
F.M.	F	70	Ca. rectum	Combined abdominoperineal; part of vagina	2 years alive
A.L.	F	60	Ca. rectosigmoid	Resection of sigmoid, adjacent peritoneum, psoas muscle	5 years alive
A.K.	F	32	Ca. sigmoid, multiple polyposis	Resection of sigmoid, colon, partial resection of abdominal wall	2 years died of metastases
F.K.	M	36	Ca. sigmoid, multiple polyposis	Resection of sigmoid, colon, partial resection of abdominal wall	2 years died of metastases
C.L.	M	68	Ca. sigmoid	Left hemicolectomy, splenectomy	5 days died of peritonitis
A.G.	F	67	Ca. sigmoid	Left hemicolectomy, splenectomy	7 years alive
M.V.	F	51	Ca. splenic flexure	Left hemicolectomy, splenectomy	5 years alive
A.M.	F	68	Ca. transverse colon	Resection of transverse colon, partial hepatectomy	1 year died of liver metastases
P.K.	M	48	Ca. cecum Ca. splenic flexure	Subtotal colectomy, total left hepatic lobectomy	13 years
G.B.	M	72	Ca. ascending colon; duodenal obstruction	Rt. hemicolectomy, partial gastrectomy, pancreatoduodenectomy	11 months died of metastases
M.P.	M	46	Ca. ascending colon, duodenocolic fistula	Rt. hemicolectomy, partial gastrectomy, pancreatoduodenectomy	2½ years died of metastases
T.G.	M	63	Ca. splenic flexure, obstruction	Colostomy, left hemicolectomy, partial gastrectomy, partial pancreatectomy, resection of one-fourth of left diaphragm, splenectomy	3 years alive

tases. The first patient had a carcinoma of the splenic flexure and a palpable nodule in the left lobe of the liver. After left hemicolectomy, the entire left lobe of the liver was resected.

TABLE II.—SUMMARY OF RESULTS OBTAINED IN RADICAL SURGERY

	No.	Per cent
Cases	21	
Hospital mortality	1	4.76
Patients surviving 10 or more years	3	14.3
Patients surviving 5 to 10 years	6	28.6
Patients surviving 2 to 5 years	5	23.8
Patients surviving less than 2 years	6	28.6
Patients surviving 2 to 13 years	14	67

Microscopic examination revealed a benign cholangioma. This patient is alive and in good health today. He has survived 13 years and has had carcinoma of the cecum, carcinoma of the splenic flexure, and 5 separate squamous cell carcinomas of the skin.

The second patient had a carcinoma of the transverse colon and a solitary nodule in the right lobe of the liver. A triangular segment of the liver was resected as well as the transverse colon and the greater omentum. One year later, at necropsy, the liver was almost completely replaced with metastases.

Carcinoma of the upper colon with contact invasion of the epigastric organs, such as duodenum, pancreas, stomach, spleen, or diaphragm, presented several challenging prob-

TABLE III.—PATIENTS ADMITTED WITH DELAYED DIAGNOSIS OR WITH DIAGNOSIS OF INOPERABLE NEOPLASM

			Two to 10 year survival after radical surgery
	No.	Per cent	Per cent
Radical surgery	21	100	67
Treated elsewhere as inoperable	5	23.8	80
Without surgical exploration	2	9.5	100
After surgical exploration	3	14.3	66.7
Delayed by misdiagnosis	3	14.3	66.7
Surgery delayed	8	38.0	75

lems. Adequate exposure was one of them. Thoracolaparotomy was used to obtain satisfactory exposure in the patient with a large carcinoma of the splenic flexure with invasion of the tail of the pancreas, spleen, stomach, and diaphragm. After resection of the mass containing parts of these organs, the diaphragm was reconstructed by suturing it to the upper edge of the thoracic wall incision, in the bed of the eighth rib. This closed the thoracic cavity long before the remaining operative procedure was completed. This maneuver did not compromise the exposure obtained by the thoracolaparotomy incision.

Another problem encountered in this group was the difficulty in determining resectability at exploration. When several organs are fused together by a neoplastic process, the bulk of the mass may obscure extensive lymphatic metastases. The patient whose invasive carcinoma of the hepatic flexure was resected by right hemicolectomy and pancreatoduodenectomy presented such a problem. After resection of the carcinoma mass, inoperable lymphatic metastases were found in the retroperitoneal area. This patient survived only 11 months. The operation inflicted was too radical. A better procedure would have been a simple gastrojejunostomy to relieve the duodenal obstruction and ileocolostomy to bypass the obstructing carcinoma of the hepatic flexure.

It may be assumed that delay in diagnosis is one of the reasons for a carcinoma reaching the advanced stage. This delay often is caused by a reluctance on the part of the patient to seek medical care. In this series, 3 cases were misdiagnosed, 5 were declared inoperable, and 13 patients did not seek medical care until the neoplasm reached the advanced stage. The survival of these patients after radical surgery is shown in Table III.

TABLE IV.—STUDY OF OPERABILITY AND RESECTABILITY IN CARCINOMA OF COLON AND RECTUM

	No.	Per cent
Cancer patients examined	230	100
Surgery not recommended	5	2.2
Patients found operable	225	97.8
Patients found not resectable	12	5.2
Patients found resectable	213	92.6
Patients with multiple organ resection	21	9.1

The diagnosis of cancer of the colon or rectum was made in 230 patients. Only 5 patients were found inoperable. The frequency with which the advanced carcinoma occurred within this series of cases is demonstrated in Table IV.

There are great differences in the rate of resectability which have been reported by various authors. A partial quotation from Bacon indicates rates of from 35 to 91 per cent (Table V).

TABLE V.—STATISTICS ON RESECTABILITY*

Name	Reported year	No. of cases	Per cent resectable
Hayden	1936	303	65–70
Hayden	1945	217	91.2
David	1936	—	00
Lahey	1936	—	70
Lahey	1946	—	83
Cattell	1943	335	83.5
Cattell	1947	—	90.7
Babcock	1937	220	77
Babcock	1946	559	97
Miles	1939	—	65
David and Gilchrist	1942	277	65.8
Vynalek	1947	486	35.6
Baker	1944	—	60
Bacon and Gass	1944	256	80.2
Bacon (Group A)	1948	800	87.7

*Quoted from: BACON, H. E. Anus, Rectum, Sigmoid Colon; Diagnosis and Treatment. 3rd ed. Philadelphia: J. B. Lippincott Co., 1949.

The reasons for these marked variations are: (1) the lack of strict adherence to the definition of the terms operability and resectability; (2) statistics obtained from charity institutions have lower rates than those reported from private hospitals; (3) hesitation on the part of many authors to report a case as resectable when the resection of the primary mass was executed as a palliative procedure. The term "operability" means any operation performed specifically for the treatment of the disease; whereas the term "resectability" refers to the actual removal of the primary neoplastic mass with either palliative or curative intent.

CONCLUSIONS

1. An extension of carcinoma of the colon and rectum into another organ or structure is not necessarily a contraindication to curative or palliative surgery.

2. The resection of the primary lesion in continuity with the involved adjacent organ or structure increased our rate of resectability by 9 per cent.

3. An exploratory dissection of a neoplastic mass without compromising blood supply may convert a seemingly hopeless mass into a resectable one. Such an exploratory dissection avoids irretrievable radicalism and diminishes the possibility of abdicative conservatism.

FRACTURE OF THE PROXIMAL PORTION OF THE TIBIA IN CHILDREN FOLLOWED BY VALGUS DEFORMITY

LEWIS COZEN, M.D., F.A.C.S., Los Angeles, California

FRACTURE of the tibial shaft in children generally is not associated with complications. This fracture is deemed innocuous especially if displacement is not concomitant. This paper records 4 instances of valgus deformity following fracture of the upper part of the tibial shaft in children. In all cases displacement of the fracture was minimal.

REPORT OF CASES

CASE 1. R.L., aged 6 years, sustained a fracture of the proximal portion of the left tibia and fibula as a result of a bicycle accident (Fig. 1). The tibia was manipulated under general anesthesia May 5, 1941, the day of the accident. A cast was applied from the toes to the groin with moderate flexion of the knee (Fig. 2). Approximately 3 years after the accident, July 20, 1944, he returned to the clinic because of severe valgus deformity which had taken place at the knee (Fig. 3a). A follow-up after December 1944 was not possible because the patient moved out of the state.

CASE 2. L.P., aged 5 years, fell while roller skating on January 28, 1950. Incomplete fractures of the proximal portion of the left tibia and of the left fibula were incurred (Fig. 4). The position was excellent and a cast was applied from the toes to the groin, with the knee flexed about 30 degrees (Fig. 5). Immobilization with a plaster cast was continued for 7 weeks, and union was solid. On removal of the plaster the position of the site of the fracture was excellent, and roentgenograms made at frequent intervals disclosed maintenance of excellent position. On clinical examination in May 1950 considerable valgus of the knee at the site of the fracture was

From the Clinics of the Orthopedic Hospital, Los Angeles.

a b

Fig. 1.

a Fig. 2. b

Fig. 1. Case 1. a, The fracture at the time of the accident. b, After application of a plaster cast immediately following the accident.

Fig. 2. Case 1. Three weeks after the accident.

a Fig. 3. b

Fig. 3. Case 1. a, Three years after the accident; there is considerable valgus without evidence of damage to the epiphyseal line. b, Correction of the valgus was performed by supracondylar osteotomy.

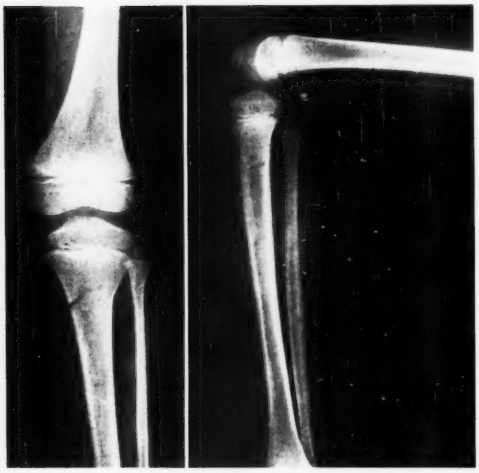


Fig. 4.

Fig. 5.

Fig. 6.

Fig. 4. Case 2. The fracture at the time of injury.
Fig. 5. Case 2. The fractured tibia encased in plaster; displacement of the fracture is not present.
Fig. 6. Case 2. Valgus deformity of the left tibia after removal of the plaster and complete union of the fractured ends. The involved leg is on the reader's right.

seen and a roentgenogram confirmed the presence of valgus deformity (Fig. 6). The valgus deformity on clinical examination was more obvious than that seen on roentgenographic examination. The patient was then seen by Dr. Harold Crowe who prescribed a long leg brace to correct the deformity. After the brace had been worn for 6 months the deformity was corrected. When last examined by Dr. Crowe on August 7, 1951, 18 months after injury, the valgus deformity had not recurred but the involved leg was ¼ inch longer by measurement from anterior-superior iliac spine to internal malleolus.

CASE 3. E.M., aged 7 years, sustained a fracture of the upper part of the tibia and of the fibula as a result of being struck by an automobile. The epiphyseal plate evidently was not involved (Fig. 7). Reduction was performed under general anesthesia, but slight valgus remained. A cast extending from the toes to the groin was worn for 5 weeks. On removal of the cast, severe valgus of the knee was noted. A brace with a valgus strap was worn at night only, and an inner wedge was used on the heel of the shoe. However, these measures were ineffective in correcting the valgus deformity after 4 months (Fig. 8).

CASE 4. M.B., aged 3 years, sustained a fracture of the upper end of the tibia on March 24, 1949, as the result of being struck by an automobile. There was no displacement of the fracture; a cast was applied from the toes to the groin (Figs. 9, 10a, and 10b). The cast was removed at the end of 7 weeks, at which time moderate valgus deformity of the knee

was noted. A long leg brace with a valgus knee strap was applied on March 3, 1950, since spontaneous correction had not occurred during the interim (Figs. 10b and 11a). On November 17, 1950, the brace was discarded since valgus deformity had almost completely disappeared (Fig. 11b). On that date the involved right tibia was ⅛ inch longer than the left. Both femurs were of equal length as measured by teleroentgenogram.

Fig. 7. Case 3. Roentgenogram of the original fracture which demonstrates that the epiphyseal line apparently is not involved.

Fig. 8. Case 3. Anterioposterior views of both tibias 6 months after the fracture occurred. The valgus deformity, as well as the increased length of the right tibia, is evident on the teleroentgenogram.

DISCUSSION

It is not the purpose of this report to describe alterations in length following fractures in children. Blount (2) and Aitken have written on this subject before. The purpose of the report is to emphasize the valgus deformity following this particular type of fracture. The author's attention has been called to the presence of several additional cases other than those which have been described, but because of medicolegal implications they cannot be reported.

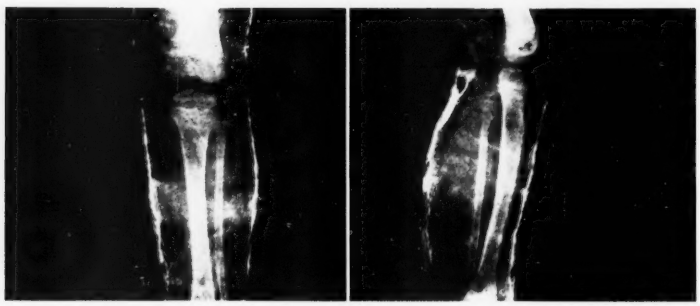
What is the cause of the valgus deformity in the cases reported? Was the original fracture reduced inadequately? In 2 cases there was no displacement; in the other 2 reduction unquestionably was adequate. Was immobilization discontinued before the fractured ends had united? This could not possibly be the cause since plaster casts, full length from toes to groin, were worn until union was solid. Was there permanent injury to the epiphyseal disc? None was evident on the roentgenograms.

Several possibilities remain. One is that stimulus to overgrowth—a well known phenomenon in fracture of growing bones—was unequal in the tibia and the fibula. If the stimulus to growth was greater in the tibia than in the fibula, valgus deformity would occur.

Blount (3) suggests the possibility of stimulation to a small portion of the epiphyseal plate as another explanation for the deformity phenomenon.

Another possible cause for the deformity might be the restraining influence of the iliotibial band. Irwin has pointed out the deforming power of this band in poliomyelitis. In healing fractures its influence may be similar. The bowstring effect of the iliotibial band may be enhanced by incomplete fracture

a



b

Fig. 9.

a b c

Fig. 10.

Fig. 9. Case 4. a, Both legs at the time of the fracture of the left tibia. b, The position of the fracture is excellent after application of the plaster without manipulation; note that the epiphyseal line is not involved.

Fig. 10. Case 4. a, b, Roentgenograms 3 weeks after the fracture demonstrate maintenance of the original excellent position. c, Ten months after the fracture was sustained, roentgenogram reveals valgus deformity of the left tibia (the left tibia is on the reader's right).

a

b

Fig. 11. Case 4. a, The amount of valgus deformity 1 year after the occurrence of a nondisplaced fracture of the upper parts of the tibia and the fibula. b, The valgus deformity is well corrected after a corrective brace was worn for 8 months.

of the fibula or surface of the tibia. In any event the deformity, following fractures in the upper third of the tibia in children, must be recognized as a real hazard. In 3 of these 4 cases malpractice litigation was threatened.

Prevention of the deformity is problematic. It may be possible to immobilize these fractures in a position of slight varus, anticipating the propensity to valgus.

Correction of the deformity, once it has occurred, may be accomplished by means of a long leg brace with a valgus strap or pad. Such a brace must be worn during the day for a period of 4 to 6 months. Osteotomy, preferably supracondylar, to prevent recurrence of the deformity, is an alternative method of treatment.

SUMMARY

Valgus deformity occurred as a complication to the healing of fracture of the proximal portion of the tibial shaft in 4 children. It is suggested that this is a complication to be expected and that the parents of the patients should be warned regarding the possibility of its occurrence. Absence of obvious injury to the epiphyseal plate does not seem to prevent this deformity.

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EXPERIMENTAL UREMIA: EXCESSIVE QUANTITIES OF PLASMA PROTEIN AND NITROGEN REMOVED IN THE OUTFLOW FLUID DURING PERITONEAL IRRIGATION OF BILATERALLY NEPHRECTOMIZED DOGS

E. E. MUIRHEAD, M.D., F. JONES, B.S., J. A. STIRMAN, M.D., and W. LESCH, B.A., Dallas, Texas

THE prolongation of the life of the dog following bilateral nephrectomy by means of dialyzing procedures, such as peritoneal irrigation, brings into focus several outstanding disturbances associated with this form of renal insufficiency and uremia. Three readily detectable and prominent disturbances have been previously emphasized, hypertension, cardiovascular lesions, and an anemia associated with a hemolytic mechanism. In the present communication we wish to describe additional significant disturbances in this experimental preparation, namely, the removal from the organism of considerable quantities of plasma protein and nonprotein nitrogen via the irrigating fluid used in the peritoneal lavage. The variations, magnitude, and other general features of the removal of protein and nitrogen by this route will be discussed. Moreover, the occurrence of hypertension, under the influence of protein and nitrogen depletion will be described.

METHODS

Adult mongrel dogs weighing 8.6 to 19.7 kilograms were used. The kidneys were removed under ether anesthesia 1 week apart by the posterior extraperitoneal approach. Peritoneal irrigation was begun on the day of the second nephrectomy. The irrigating technique and the composition of the irrigating fluid have been described elsewhere (5). The daily volume of fluid removed from the peritoneal cavity varied between 1,000 and 6,800 cubic centimeters; the usual volume varied between 2,000 and 4,000 cubic centimeters.

The diet consisted of a semisolid formula containing peanut oil, glucose, protein, and vitamin supplements, as previously described (5). The protein intake varied between 0.5 and 3.5 grams per kilogram body weight per day. The total caloric intake and its relation to the nitrogen intake and output are considered later.

The total protein concentration of the daily pool of irrigating fluid removed was determined by the Greenberg method which had been standardized by the micro-Kjeldahl and nesslerization technique. The nitrogen concentration of the fluid was determined by microdigestion, direct nesslerization and colorimetric determination. The blood urea was determined by the method described by Taylor and Blair. Fractionation of the plasma and peritoneal fluid proteins was accomplished by the precipitation method of Kibrick and Blonstein. The electrophoretic patterns were conducted with the following conditions: electrophoretic analyses were made in a Tiselius apparatus having a single sectional microcell of 2 milliliter capacity. Each serum sample was previously diluted with 3 volumes of 0.02 molar sodium phosphate buffer, *p*H 7.4, and containing 0.15 molar sodium chloride. Samples of peritoneal lavage were analyzed undiluted. Before analysis both serum and peritoneal lavage samples were dialyzed against large volumes of the buffer which was also used to fill the electrode vessels of the apparatus. Pictures of the protein patterns were taken using the Longsworth scanning method

From the Department of Pathology, Southwestern Medical School of the University of Texas, Dallas, Texas. Supported by a grant from the U. S. Public Health Service, National Heart Institute.

TABLE I.—FREQUENCY DISTRIBUTION OF THE DAILY PROTEIN CONCENTRATION WITHIN THE OUTFLOW PERITONEAL FLUID (19 DOGS)

Concentration gm./L.	No. of observations
>1	3
1	36
2	42
3	26
4	44
5	22
6	12
7	3
8	5
9	7
10	0
11	1
12	2
13	1

Mean = 4.08 gm./liter

after 1 hour of electrolysis with a field strength of 4.2 volts per centimeter. The plasma volume was determined with the T-1824 dye according to Mayerson and co-workers. The mean arterial pressure was obtained by means of direct femoral artery puncture and a mercury manometer.

The various observations were conducted during the first 15 days after the removal of the second kidney.

PLASMA PROTEIN IN THE OUTFLOW FLUID DURING PERITONEAL IRRIGATION

Total protein concentration in peritoneal fluid. The variations of the total protein concentration in the outflow fluid from the peritoneum up to 15 days after the second nephrectomy are exemplified by the 10 examples depicted in Figure 1. Four general groups are demonstrated. In the first group of 3 dogs the protein concentration varied mainly between 1 and 3 grams per liter. In the second and third groups of 3 dogs each, the concentration varied mainly between 3 and 5 and 5 and 7 grams per liter respectively. In the last group of 1 dog the concentrations were mainly between 8 and 12 grams per liter. Nine additional dogs, not depicted in the figure, had concentrations of protein varying between 2.5 and 6 grams per liter. Thus, the protein concentration remained within certain ranges and appeared to represent in part, an individual characteristic of the animals. While in some animals there was a slight elevation of the protein concentration during the first 3 days, as from 1 to 3 or from 2.5 to 4 grams per liter, in others the concentration remained fairly steady throughout. In all animals the general range of concentration obtained throughout the 15 days was indicated by the concentration within the first 3 days.

TABLE II.—TOTAL PLASMA PROTEIN IN PERITONEAL FLUID EXPRESSED AS GRAMS PER DAY PER KILOGRAM WEIGHT

gm./kgm./day	No. of dogs
0.5	6
0.7	3
0.9	4
1.1	2
1.3	1

Mean = 1.03 gm./kgm./day
Mean weight = 13.1 kgm.
Aver. amt., 12.6 gm./day

An additional expression of the protein concentration within this artificial form of ascites is related by the frequency distribution of all daily protein concentrations of the 19 dogs given in Table I. The mean value was 4.08 grams per liter ($\sigma \pm 2.0$).

Total protein in peritoneal fluid. The total quantity of protein removed from the animals each day by the peritoneal irrigation naturally was an expression of the protein concentration and the total volume of fluid removed. With these animals the total volume of fluid removed per day varied between 1 and 6.8 liters (usually 2 to 4 liters), thus, the total quantity of protein removed varied between 1 and 65 grams per day. In Table II is related the frequency distribution of the protein removed from 16 dogs expressed as grams of protein removed per kilogram per day. The values varied between 0.5 and 1.3 grams per kilogram per day with an average of 1.03 grams per kilogram per day. The average weight of the 16 dogs was 13.1 kilograms. The mean daily loss of plasma protein by this route, as averaged from the individual figures, was 12.6 grams, a quantity representing about one-third of the average total quantity of circulating plasma proteins.

Circulating plasma protein concentration. The variations in the circulating plasma protein concentration in 18 dogs are depicted in Figure 2. There was an average decrement in concentration of 1.3 grams per 100 cubic centi-

meters of plasma. The hypoproteinemia occurred in the absence as well as in the presence of weight loss. As related in Figure 2, the main decrement occurred during the first week, thereafter further decrements tended to be less pronounced. Below it will be pointed out that the hypoproteinemia resulted mainly from a recession in the plasma albumin concentration.

Changes in the protein fractions of the circulating plasma. The protein of the circulating plasma was fractionated by the method of Kibrick and Blonstein on the first day and about 1 week after the second nephrectomy. The results from 9 dogs are summarized in Table III. The alpha globulin fraction was slightly increased in 6 and slightly lowered in 3 animals giving a minimal increment in the average figure. The beta globulin fraction was slightly decreased in 7, slightly increased in 1, and unchanged in 1, giving an average figure indicating an over-all slight decrease in this fraction. The gamma globulin fraction was as often decreased as increased, the average being slightly increased. When the globulins were totaled they were only slightly lowered in concentration during the first 2 weeks following bilateral nephrectomy.

As mentioned previously, the total protein concentration was lowered by over 1 gram per 100 cubic centimeters. This resulted mainly from a decrement in the albumin concentration (average minus 0.9 gm. per 100 c.c.), although the fibrinogen concentration was also lowered.

Changes in the protein fractions of the peritoneal fluid. All protein fractions in the outflow peritoneal fluid increased in concentration during the first 2 weeks (Table IV, same 9 dogs as in Table III). The increments in alpha and gamma globulin exceeded those of beta globulin. The fibrinogen and albumin concentrations in the fluid were distinctly elevated. The fractionation properties as well as the electrophoretic mobility of the proteins indicated their source from plasma protein.

Plasma: peritoneal fluid ratio of various protein fractions. The ratio of the various protein fractions in the plasma to the fluid underwent a marked change due to the alterations in the various concentrations mentioned. In general the fractions in the circulating plasma decreased while those in the fluid increased culminating in a prominent drop in the ratio as follows: alpha globulin, −63 per cent; beta globulin, −60 per cent; gamma globulin, −51 per cent; fibrinogen, −39 per cent; albumin, −58 per cent; total protein, −56 per cent.

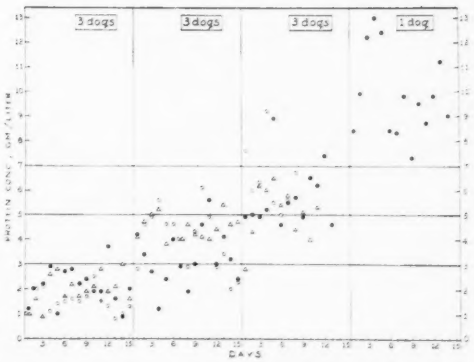

Fig. 1. The figure depicts the protein concentration in the outflow peritoneal irrigation fluid, expressed as grams per liter. The observations were conducted up to 15 days. The horizontal lines isolate the main ranges 1 to 3, 3 to 5, 5 to 7, and 8 to 12 grams per liter. Four groups falling mainly within these ranges are shown. The open circle, solid dot, and triangle indicate the values for individual dogs.

Electrophoretic pattern of plasma and peritoneal fluid. Electrophoretic patterns were obtained from simultaneous samples of plasma and fluid in 8 dogs. These were obtained on

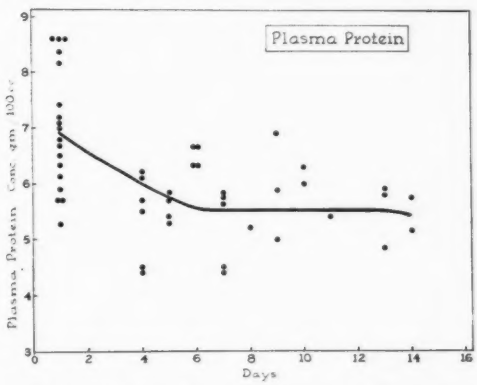

Fig. 2. The plasma protein concentration, expressed as grams per 100 cubic centimeters, during the course of daily intermittent peritoneal irrigation of nephrectomized dogs. The mean curve indicates a hypoproteinemia which developed mainly during the first week after the second nephrectomy.

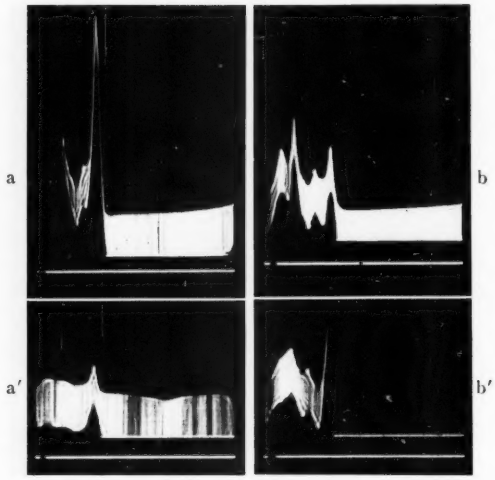

Fig. 3. Electrophoretic patterns of serum and fluid obtained the same day are shown. a and a′ represent the serum and fluid patterns on the first day. b and b′ represent the serum and fluid patterns 1 week later. Further comments in the text.

TABLE III.—CHANGES IN THE PROTEIN FRACTIONS OF THE CIRCULATING PLASMA, GRAMS PER LITER

Protein	I First day	II After 5–9 days	Ratio I/II
Alpha globulin	7.5–19.0	6.5–22.0	0.8–1.2
	av. 14.0	av. 15.6	av. 0.98
Beta globulin	5.5–12.0	3.6–8.3	0.7–1.9
	av. 7.7	av. 6.2	av. 1.3
Gamma globulin	5.0–10.0	5.0–17.0	0.5–1.8
	av. 6.5	av. 6.7	av. 0.93
Fibrinogen	6.3–10.6	2.1–9.9	0.6–5.0
	av. 7.7	av. 5.5	av. 1.9
Total globulins	28–40	27–42	0.8–1.5
	av. 36.0	av. 33.0	av. 1.09
Albumin	20–39	16–24	1–1.6
	av. 29.0	av. 20.0	av. 1.4
Total protein	57–72	45–63	1.1–1.5
	av. 65.0	av. 54.0	av. 1.2

the first day and about 1 week later. A typical example of the ascending boundary is given in Figure 3. These observations corroborated the fractionation findings obtained by the precipitation method. Thus, it can be noted that on the first day (patterns a and a′) the usual peaks are noted for the plasma proteins whereas the fluid had mainly an albumin peak and a minor globulin-fibrinogen zone. One week later, however, marked changes occurred (patterns b and b′). The plasma albumin peak is lower while the globulins remain prominent. In the fluid, on the other hand, the prominence of the albumin and globulin-fibrinogen zone made for a pattern resembling that of the plasma more clearly. Similar observations were noted in the 8 dogs studied. The changes in the pattern of the proteins in the plasma suggest changes in the configuration of the molecules which conceivably could influence the diffusion through the peritoneum. This possibility is being considered.

Changes in total circulating plasma protein versus plasma protein loss via the irrigating fluid: evidence for considerable generation of plasma protein. The total circulating plasma protein was determined by the plasma volume as estimated by the T-1824 dye method and the total plasma protein concentration. Determinations were conducted before and 1 to 2 weeks after the second nephrectomy. During the same intervals the total quantity of plasma protein removed via the outflow peritoneal fluid was determined by volume measurement and the measurement of the protein concentration of pooled 24 hour collections. In Table V the results in 12 dogs have been reduced to the quantities involved per day. It is apparent in Table V that the total quantity of circulating plasma proteins was either unchanged or actually increased in 50 per cent of the dogs while at the same time considerable quantities of plasma protein were being lost in the irrigating fluid. In the remaining 50 per cent of the dogs the total amount of plasma proteins decreased but to an extent far lower than expected in accordance with the quantities removed in the irrigating fluid. The differences between these two sets of data are so great as to indicate a considerable production of plasma protein during the intervals involved. According to these data, the quantities of plasma protein produced per day varied between 6 and almost 40 grams. The mean figures would indicate an average production of 0.92 gram of plasma protein per kilogram

TABLE IV.—CHANGES IN THE PROTEIN FRACTIONS OF THE PERITONEAL FLUID, GRAMS PER LITER

Protein	I First day	II After 5–9 days	Ratio I/II
Alpha globulin	0.05–0.94	0.7–0.15	0.05–0.46
	av. 0.38	av. 1.0	av. 0.3
Beta globulin	0.03–0.38	0.16–0.55	0.03–0.78
	av. 0.2	av. 0.44	av. 0.4
Gamma globulin	0.18–0.87	0.2–2.0	0.2–1.7
	av. 0.4	av. 0.76	av. 0.84
Fibrinogen	0.28–1.63	0.3–4.8	0.16–1.1
	av. 0.7	av. 1.3	av. 0.75
Total globulins	1.0–3.1	2.0–6.3	0.14–0.8
	av. 1.6	av. 3.5	av. 0.5
Albumin	0.7–3.0	1.6–3.8	0.24–1.3
	av. 1.5	av. 2.4	av. 0.63
Total Protein	2.0–6.3	3.7–9.4	0.22–0.74
	av. 3.1	av. 6.0	av. 0.5

TABLE V.—RELATIONSHIP OF CHANGES IN TOTAL PLASMA PROTEIN AND PROTEIN CONCENTRATION TO AMOUNT OF PROTEIN LOSS IN FLUID

Dog No.	Body wt. before second nephrectomy, kgm.	No. days for observations	Change in total plasma protein[1] gm./day	Protein loss in fluid (average)[2] gm./day	Plasma protein produced (average)[3] gm./day
1	13.2	15	+2.2	6.9	9.1
2	13.9	13	−3.5	9.2	5.7
3	11.8	13	−1.4	15.1	13.7
4	18.8	15	0	20.2	20.2
5	13.6	15	−1.8	41.0	39.2
6	9.0	6	+2.6	5.0	7.5
7	11.3	7	−1.4	14.5	13.1
8	13.4	8	−1.0	11.0	10.0
9	16.5	5	0	7.8	7.8
10	10.8	5	0	9.0	9.0
11	15.5	7	−1.7	8.0	6.3
12	15.5	7	0	9.0	9.0
Average	13.6	9.6	−0.5	13.1	12.6

[1] (Plasma vol. × plasma protein conc.)$_2$—(Plasma vol. × plasma protein conc.)$_1$ ÷ No. days 1 to 2
[2] Daily addition of (vol. peritoneal fluid × protein conc.) ÷ No. days
[3] Total protein in fluid (7–15 days)—Decrement total plasma protein ÷ No. days

body weight per day. Thus, a considerable segment of the protein economy of the body appeared to be directed toward the production of plasma protein, in a manner and magnitude comparable to that encountered in dogs severely depleted of plasma proteins by plasmapheresis.

Summary of changes related to plasma proteins.—The following observations have been made on the plasma proteins in the circulating plasma and outflow peritoneal fluid during intermittent peritoneal irrigation of bilaterally nephrectomized dogs for intervals up to 15 days: (1) The total protein concentration of the outflow fluid varied between 1 and 13 grams per liter (average 4 grams per liter) but tended to remain within relatively narrow ranges as an apparent individual dog characteristic. (2) Due to the volumes of fluid removed by the irrigating procedure considerable quantities of protein were removed from the organism each day, the mean figure indicated a loss of nearly 1 gram per kilogram per day. (3) The circulating plasma protein concentration was reduced by an average of 1.3 grams per 100 cubic centimeters, mostly within 1 week; the reduction was due mainly to a decrement in the plasma albumin concentration. (4) By fractionation and electrophoretic studies the protein in the outflow fluid was identified as plasma protein. (5) In the course of the irrigating procedure and the uremia the concentrations of the plasma globulin fractions (alpha, beta, gamma) were slightly and inconsistently disturbed while the plasma fibrinogen and albumin concentrations were significantly lowered, while at the same time the concentration of all globulins, fibrinogen, and albumin in the outflow fluid were increased; yet, the total protein concentration in the outflow fluid remained relatively low, thus suggesting a minor increase in permeability to proteins or a greater diffusion of altered protein molecules. (6) Evidence was obtained indicating a considerable generation of plasma proteins during the course of the peritoneal irrigation in association with the removal of protein in the irrigating fluid.

TOTAL NITROGEN IN THE OUTFLOW FLUID DURING PERITONEAL IRRIGATION

Total nitrogen concentration in the peritoneal fluid. There was a marked variation in the nitrogen concentration of the peritoneal fluid

TABLE VI.—THE FREQUENCY DISTRIBUTION OF THE DAILY TOTAL NITROGEN CONCENTRATION OF THE OUTFLOW FLUID

(23 Dogs)

Nitrogen conc. gm./liter	No. of determinations
1	14
2	17
3	31
4	29
5	28
6	28
7	28
8	14
9	15
10	4
11	1
12	1
13	1

Mean = 5.8 gm./liter
$\sigma \pm 2.5$

of different dogs. As with the protein concentration the concentration remained within certain ranges. This feature is exemplified by Figure 4 wherein the results from 16 dogs are depicted. There was a tendency for the nitrogen concentration to increase as the nitrogenous retention progressed, but, even so, in the first group of 4 dogs the concentration remained mostly between 1 and 4 grams per liter, in the second group of 8 dogs the concentration was mainly between 3 and 7 grams per liter, and in the third group of 4 dogs the concentrations were mainly between 6 and 11 grams per liter.

Table VI depicts the frequency distribution of the daily nitrogen concentrations of the outflow peritoneal fluid as observed in 23 dogs. The mean value was 5.8 grams per liter with a considerable spread on each side of this value (1 to 13 grams per liter).

TABLE VII.—THE TOTAL NITROGEN IN PERITONEAL FLUID IS EXPRESSED AS GRAMS PER DAY PER KILOGRAM WEIGHT

gm./kgm./day	No. of dogs
0.3	1
0.5	5
0.7	3
0.9	3
1.1	1
1.3	1
1.5	1
2.1	1

Mean = 0.9 gm./kgm./day
Mean weight = 13.1 kgm.
Aver. amt., 11.5 gm./day

TABLE VIII.—THE FREQUENCY DISTRIBUTION OF THE NEGATIVE NITROGEN BALANCE IS TABULATED AS THE INCIDENCE OF THE NET LOSS OF NITROGEN EXPRESSED AS MINUS GRAMS OF NITROGEN PER KILOGRAM OF BODY WEIGHT PER DAY

Net loss of nitrogen gm./kgm./day	No. of dogs
0.2	1
0.2	0
0.4	4
0.6	6
0.8	3
1.0	3
1.2	0
1.4	1
1.6	0
1.8	1

Mean = 0.82 gm. N_2/kgm./day
$\sigma \pm 0.39$
Aver. weight, 13.4 kgm.
Aver. loss N_2—10.2 gm./day

Total nitrogen in the peritoneal fluid. The total quantity of nitrogen removed from the organism per day depended partly on the volume of fluid removed. Usually 2 to 4 liters were recovered per day. Table VII gives the frequency distribution of the average quantity of nitrogen removed per day from 16 dogs. The mean value was 0.9 gram per kilogram per day. The average total amount of nitrogen removed per day was 11.5 grams. These figures indicate that these animals lost a considerable amount of nitrogen in the peritoneal fluid.

Nitrogen balance and caloric intake. The average caloric intake for the present series of dogs was 40 calories per kilogram body weight per day, however, most animals received between 35 and 55 calories per kilogram per day. Although the caloric intake derived from protein varied between 5 and 33 per cent of the total, in 90 per cent of the animals the protein fraction varied between 5 and 10 per cent of the caloric intake. Essentially the intake of protein was subnormal and most of the calories in the diet were derived from fat (peanut oil) and glucose. Vomiting was frequently minimal or absent, being troublesome in an occasional animal. The dietary formula was given in small quantities 2 to 3 times daily. In about 1 of 7 days the feedings were withheld in order to perform certain tests. Between one-fourth to one-third of the caloric intake

was derived from glucose absorbed from the irrigating fluid via the peritoneal surfaces. Thus, these animals were adequately supplied with calories, and yet, despite a satisfactory indication of lack of starvation a markedly negative nitrogen balance developed.

The nitrogen balance was determined by the total protein intake by mouth and the nitrogen output via the peritoneal fluid and feces. Table VIII expressed the net loss of nitrogen as grams per kilogram per day as determined in 19 dogs during the first 2 weeks after the second nephrectomy. Eighty-five per cent of these animals displayed a negative nitrogen balance amounting to 0.4 to 1 gram of nitrogen per kilogram per day. The over-all mean figure indicated a loss of 0.82 gram of nitrogen per kilogram per day. The average weight of these animals was 13.4 kilogram. When the measured total negative nitrogen figures were totaled and averaged it was determined that the mean daily negative balance of nitrogen amounted to 10.2 grams. It is evident that in these experiments the quantities of calories in the diet did not avert a major degree of nitrogen loss and that the intake of protein was grossly disproportionate to the dissipation of nitrogen.

Changes in body weight. The animals were weighed each morning following the removal of the overnight peritoneal fluid. Changes in weight of such animals are greatly dependent on the amount of fluid which is allowed to be absorbed by the peritoneal surfaces. The absorption of fluid in turn is greatly dependent on the osmolarity of the irrigating fluid. By increasing the concentration of the fluid, as with glucose, it is possible to maintain a rigid fluid balance for varying intervals. With most animals in the present experiments no attempt was made to maintain a strict fluid balance, as a consequence, most animals gained weight, especially during the first week. Some animals either maintained a steady weight or lost weight during the first week. By the second week, however, most animals lost weight. These changes are illustrated in Figure 5 which contains data from 17 dogs in which these described studies were conducted.

Since the examples in Figure 5 were demonstrated to have been in a prominent degree of

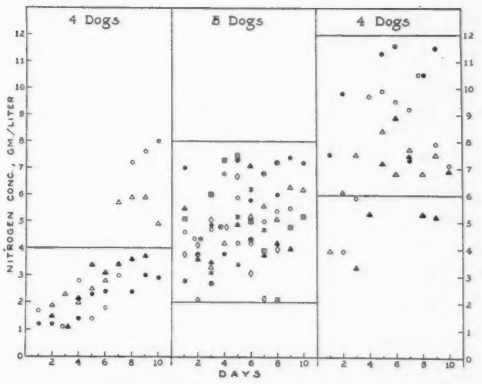

Fig. 4. The total nitrogen concentration of the daily peritoneal fluid in three groups of dogs is depicted. The individual animals are represented by the different symbols. The horizontal lines bracket the main ranges, 1 to 4, 3 to 7, and 6 to 11 grams per liter. These observations were conducted up to 10 days.

negative nitrogen balance, it is apparent that the weight gain must have been due to a gain in fluid. Those animals that failed to lose weight or appeared in a clinical state of steady nutrition must have traded a considerable amount of body substance for fluid. Despite

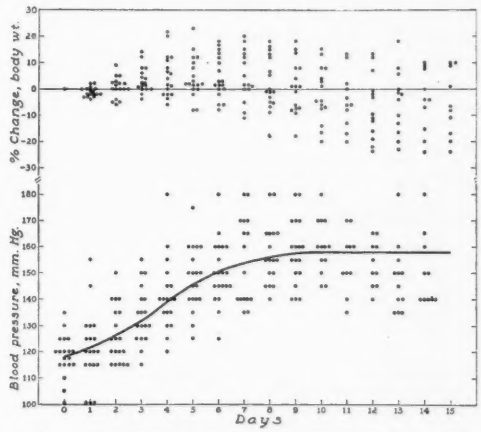

Fig. 5. The lower figure is a scattergraph of the daily mean arterial pressure. The solid line represents the mean curve for the entire group. The mean values were elevated from 115 to 155 millimeters of mercury in 7 days. The upper figure relates the changes in body weight expressed as percentile deviations from the control value which is depicted as the zero horizontal line. In general weight gain occurred during the first week and weight loss occurred thereafter.

the latter mechanism, loss of weight eventually occurred.

Hypertension, its development under the conditions described. The mean arterial pressure was taken by direct femoral artery puncture and a mercury manometer once or twice daily after withdrawal of the peritoneal fluid. The animals were subjected to a training period for this purpose prior to the second nephrectomy, during which time the control pressures were taken.

Animals subjected to peritoneal irrigation and demonstrating the described losses of plasma protein and nitrogen nevertheless under the conditions of these experiments developed a prominent degree of sustained hypertension (Figure 5). In Figure 5 the mean curve of the mean arterial pressure of 19 dogs can be seen to ascend gradually to maximum within about 7 days. The mean increment amounted to 40 millimeters of mercury indicating that in some instances the hypertension was quite pronounced.

The hypertension occurred during the interval when the body weight and fluid balance figures indicated a prominent gain in weight due to a gain in fluid. The hypertension remained prominent despite the ultimate loss of weight. Thus, it appears evident that the considerable loss of plasma protein and outpouring of nitrogen did not prevent the development of hypertension when the animals were allowed to absorb water and electrolyte (mainly sodium) from the irrigating fluid through the peritoneal surfaces.

Summary of changes related to the nitrogen output in the irrigating fluid.—The following observations concerning the total nitrogen in the irrigating fluid were made: (1) the total nitrogen concentration in the outflow fluid varied between 1 and 13 grams per liter (mean 5.8 grams per liter); while the nitrogen concentration usually increased as the uremia progressed, it nevertheless tended to remain within certain wide ranges; (2) in view of the volumes of fluid obtained from the peritoneal cavity considerable quantities of nitrogen were removed from the body, the mean figure indicated the removal of 0.9 gram per kilogram body weight per day; (3) the caloric intake by mouth and via the peritoneal surfaces, consisting mainly of fat and carbohydrate, were ample to prevent excessive endogenous protein breakdown, yet in the absence of starvation a pronounced negative nitrogen balance occurred as most animals lost between 0.4 and 1 gram of nitrogen per kilogram body weight per day; (4) although most of these animals were allowed to gain weight by means of the absorption of minor fractions of the peritoneal fluid each day, most animals eventually lost weight; it was apparent that certain animals maintained their weight by exchanging body substance for peritoneal fluid; (5) a significant hypertension developed despite the losses of plasma protein and nitrogen when the animals were allowed to absorb water and electrolytes (mainly sodium salts).

DISCUSSION

The protein in the outflow fluid from the peritoneum, which had the fractionation and electrophoretic characteristics of plasma protein, attained a range of concentration after equilibrium that was quite distinct from that of inflammatory exudates or of the edema fluid associated with burns and trauma which have concentrations of the order of 3 grams per 100 cubic centimeters or higher (30 grams per liter or more). The protein concentration of the ascitic fluid of cirrhosis amounts to 1.2 grams per 100 cubic centimeters $\pm$ 0.12 gram (12 grams per liter $\pm$ 1.2 grams). The concentrations of exudates were never attained in the irrigation fluid and the ascitic fluid concentrations were encountered in only 1 of 19 dogs. The protein concentration of the irrigating fluid, on the other hand, was similar to that of various edema fluids as determined by Stead and Warren. The fluids analyzed by these workers were obtained from the edema of normal subjects induced by an elevated venous pressure (protein 4 to 13 grams per liter, average 8 grams per liter); from the edema of cardiac patients (0.3 to 6 grams per liter, average 2.4 grams per liter); from the edema in patients with anoxemia (1 to 2 grams per liter); from the edema of patients with fever (3 to 9 grams per liter); and from the edema of glomerulonephritis (1 to 11 grams per liter, average 4 to 8 grams per liter). These figures compare favorably with the range of 1 to 13

grams per liter (average 4 grams per liter) obtained in the peritoneal fluid in the present series. Thus, the irrigating fluid upon withdrawal had certain characteristics of a transudate. In this respect, the fluid seemed to represent an expanded segment of the extracellular fluid. It might be entertained that the protein in the fluid was derived from an exudate which became greatly diluted. Even so, one would expect greater concentration and a more pronounced hypoproteinemia. Moreover, it would be unusual for such a mechanism to evoke a rather constant concentration.

The tendency for the protein concentrations to remain within relatively narrow ranges plus the fact that the initial or nearly the initial concentration was frequently maintained for 15 days are observations that oppose the possibility of an increased permeability to protein through capillaries. The only indication of an increase in permeability to proteins was the finding that the concentration of globulin, fibrinogen, and albumin in the fluid in some animals doubled during the 15 days of observations, even though the total protein concentration remained relatively low. Whether these minor increments resulted from a local irritation of the peritoneum or were due to the uremic state could not be determined. In view of the apparent changes in the mobility of the proteins in the Tiselius apparatus, it is conceivable that smaller more mobile mean protein molecules resulted from the uremia which, in turn, traversed the peritoneal surfaces more readily. Additional observations are needed on this point. At best there seemed to be only a subtle indication of increased permeability to proteins at the peritoneum.

The total quantity of plasma protein recovered in the fluid each day (average 1 gram per kilogram per day) was of a magnitude removed in the plasmapheresis experiments of Madden and Whipple. It is, therefore, of interest that the decrement in plasma protein concentrations, which was due mainly to a lowering of the albumin fraction, described a course similar to that during plasmapheresis, namely that the main recession in protein concentration occurred during the first week whereas thereafter the regression was much slower. A tendency toward a true hypoproteinemia was demonstrated by the estimations of the total circulating plasma proteins which were depressed in half of the animals.

During the 15 days of observations the total quantity of plasma protein removed by the irrigating fluid varied between 2.3 and 13 times the initial total quantity of circulating plasma proteins. While this substantial quantity of protein was being removed the plasma protein concentration was maintained usually at a level near 80 per cent of the control. This combination of findings alone indicated a considerable deviation of protein toward the production of plasma protein. The latter conclusion was strongly supported by the estimates of the plasma volume which indicated either no decrement or a relatively low decrement of total plasma protein despite the considerable loss via the irrigating fluid. By taking into account the protein lost in the fluid and the state of the total plasma proteins it was estimated that the animals produced an average of 0.92 gram of plasma protein per kilogram body weight per day. Thus, a substantial segment of the protein economy of the body in this form of uremia was directed toward the production of plasma protein, as discussed by Madden and Whipple in association with plasmapheresis. These observations suggest that the changes in plasma protein usually ascribed to the injury reaction did not pertain in these experiments.

Under a dietary regimen which should have been sufficient to prevent an excessive endogenous breakdown of protein, using the response of the intact animal as a reference, there occurred, nevertheless, a pronounced negative nitrogen balance. Under conditions in which hypoproteinemia and body wastage were in progress the absorption of the balanced crystalloid solution from the peritoneum readily occurred, unless stringent precautions were taken to avert this by properly increasing the concentration of the fluid. Thus, most animals in the present series either gained weight or failed to lose weight during the first week despite the prominent negative nitrogen balance. In either of these events the nitrogen measurement plus the relatively low protein intake indicated that an exchange of fluid for

body substance usually occurred. Under these conditions a significant hypertension occurred.

The observations herein reported not only demonstrate certain additional disturbances developing in the course of the experimental uremia of the dog after bilateral nephrectomy supported by in vivo dialysis which require further consideration, but also have indicated the need to re-evaluate the role of protein metabolism in the hypertension occurring under certain conditions in such preparations. Such observations are now in progress.

CONCLUSIONS

1. During peritoneal irrigation of bilaterally nephrectomized dogs the protein concentration of the outflow fluid remained within certain relatively narrow ranges; the over-all range of concentration was 1 to 13 grams per liter (average 4 grams per liter). By its protein concentration the fluid resembled the extracellular fluid encountered in the transudates of certain edematous states.

2. Fractionation and electrophoretic studies indicated that the source of the protein in fluid was plasma protein. There was only a minor indication of increase in the permeability of capillaries to protein.

3. The quantity of protein removed via the irrigating fluid was substantial. This protein drain was associated with evidence of considerable generation of plasma protein, similar to that which was observed during plasmapheresis.

4. With a normal or low protein intake a prominent negative nitrogen balance occurred. With hypoproteinemia and body wastage, absorption of fluid through the peritoneal surface readily occurred.

5. When the animals were allowed to absorb fluid, hypertension occurred despite the prominent losses of plasma protein and nitrogen. Further observations on the role of protein metabolism in the pathogenesis of this hypertension are indicated.

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WAR WOUNDS OF THE CHEST AMONG MARINE AND NAVAL CASUALTIES IN KOREA

JAMES D. KING, M.D., M.Sc., Ph.D. (Surgery), Commander, M.C., U.S.N.,
Bainbridge, Maryland, and
JAMES H. HARRIS, M.D., Lieutenant, M.C., U.S.N.,
San Diego, California

NUMEROUS reports have demonstrated the much lower mortality of thoracic wounds in World War II when compared with all previous wars. From the start of the Korean Incident early and effective application of the many lessons recently learned was possible. It might reasonably be expected, therefore, that thoracic wounds would be better cared for and the results would reflect these surgical improvements. It is the purpose of this paper to report the surgical experiences in handling 405 major thoracic casualties from Korea treated in a large Naval Hospital overseas between August 1950 and March 1952.

Mortality from chest wounds varies directly with the nature of the fighting, administrative management, early recognition, extent of first aid, and priority of evacuation to special centers. In order to understand well the opinions to be presented herein it is necessary to be somewhat familiar with the line of evacuation involving Marine Corps and Navy casualties in Korea.

The Navy maintained only a small 70 bed dispensary in Yokosuka, Japan, prior to the outbreak of the Korean War. The Army, on the other hand, had several large general hospitals, strategically located. The availability of medical and surgical services for Navy and Marine Corps casualties, then, was curtailed by the difficulties concomitantly involved in expanding hospital facilities. The dispensary was enlarged and commissioned as a naval hospital in September 1950.

The mission of this hospital was to serve as a unit for definitive treatment of Navy and Marine Corps personnel in Japan and Korea. By December 1950, the expansion was reflected in a growth of from 70 beds to facilities for nearly 5,000 patients. All of the casualties came to Yokosuka by air or sea transportation; a few came through the Army chain of evacuation. The seaborne evacuation from Korea was principally accomplished in 3 Navy hospital ships, in shuttle relays between Korea and Japan. The average elapsed time from Korea to Yokosuka involved about 3 days by ship and 4 to 5 hours by air.

Complete control of the sea and air around Korea by U. N. Forces resulted in only minor fleet action. Some casualties resulted from underwater mine explosions and shelling from enemy shore batteries. However, more than 95 per cent of our casualties were marines.

The Army, geared to land action, has a long established hospital evacuation chain, including general and evacuation hospitals. The Marine Corps, adapted normally for beachhead action, is not basically provided with an elaborate land evacuation system. In actual practice, the majority of the major Marine Corps casualties were evacuated directly from forward areas by air to Japan.

The 5 medical companies, staffed with Navy medical personnel, normally a part of the Marine Corps division, form the principal axis on which casualty treatment and evacuation are accomplished. In Korea, the Navy supplemented these available medical services with several surgical teams, consisting of from 3 to 5 surgeons and up to 10 hospital corpsmen. These teams were permanently assigned to U. S. Naval Hospital, Yokosuka, but temporarily attached to the First Marine Division. The division surgeon placed the teams with medical companies where they were most needed as particularly heavy losses occurred.

From the Department of General and Thoracic Surgery, U. S. Naval Hospital, Yokosuka, Japan.

The opinions contained herein are the private ones of the writers and are not to be construed as official, or reflecting the views of the Navy Department or the Naval Service at Large.

TABLE I.—MAJOR OPERATIONS PERFORMED

Operations	No. of cases
Thoracotomy	52
Intercostal tube drainage	33
Intrathoracic bleeding	1
Removal of bullets and fragments	8
Drainage of empyema	1
Pulmonary decortication	4
Lobectomies	4
Repair of diaphragm	1
Thoracoabdominal explorations	3
Closure of sucking chest wounds	19
Tracheotomy	2
Bronchoscopy	1
Laparotomy	43
Repair of lacerated liver	9
Colostomy	8
Splenectomy	6
Repair of diaphragm	6
Repair of kidney	5
Repair of stomach	4
Repair of intestine	3
Intestinal obstruction—mechanical	1
Removal of fragments	1
Ligation axillary vessels	3
Craniotomy (for compound skull fracture)	1
Amputation arm	1

The number of teams in the field at any given time varied with the existing military situation.

An adequate understanding of anatomy and physiology is necessary for the proper management of chest injuries. From the beginning we accepted the principles of early and rapid re-expansion of the lungs and of initial conservative management in the treatment of thoracic injuries. The material for this study was obtained by a careful review of the patients' field records, records of previous hospitalization, serial roentgenograms as presented by the patients at the time of admission to the hospital, and a careful analysis of the progress of the patients during their period of hospitalization.

This study comprises only wounds which had either perforated or penetrated the closed pleural space and involved the intrathoracic viscera. All patients were adult males ranging in age from 18 to 36 years. The average age was 20 years. The average time interval from battlefield to arrival at Yokosuka was 7 days; the shortest time elapse was less than 24 hours. Of the total 405 chest wounds, 219 resulted from small arms; 169 from grenades, mortar and artillery shells; 16 from contusion; and 1 from blast injury.

TREATMENT INSTITUTED PRIOR TO ARRIVAL AT YOKOSUKA

Thoracentesis. Thoracentesis was accomplished on 124 patients; a total of 347 thoracenteses were done and in each case an average of 2.8 aspirations. The average amount of blood removed from each patient was 939 cubic centimeters.

Major operative procedure. The number of surgical procedures performed in the forward medical facilities is listed in Table I.

The patients in this series represent those whose physical condition was best among all age groups. Undoubtedly, this excellent physical condition was an important factor in their ultimate recovery from severe trauma. The time interval from battlefield to hospital must always be influenced by the conditions and circumstances that govern the prevailing tactical situation and terrain of the country. The evacuation of the wounded in Korea was slowed by the rugged topography and lack of good highways and railroads, which largely accounted for the high average number of elapsed days before arriving at Yokosuka.

The practice of using helicopters for air evacuation from the forward areas should reduce the average evacuation time. In general, our combat casualties have resulted from small arms fire, hand grenades, mortar and artillery shells. The enemy so far has not used aerial bombing, flamethrowers, and other devices of destruction. This fact has accounted in the main for the type of casualty received.

On the basis of our own experience in the handling of cases of hemothorax, the number of patients and the number of thoracenteses done on each patient prior to arriving at Yokosuka left much to be desired. On only 124 patients, or about 30 per cent, had chest aspiration been done; and 2 aspirations usually were done in each patient. Of the patients included in Table I, only 18 had received major chest surgery in forward areas. The low figure indicates that the overall practice in the forward area in handling chest wounds has been conservative. Forty-three laporatomies were performed and all were on patients with thoracoabdominal wounds.

There were no trained thoracic surgical teams in the forward areas. The majority of

the medical officers were reserves recalled while still under residency training in civilian hospitals. However, in spite of obvious lack of experience and the usual early errors in surgical judgment, the overall understanding of war surgery and the early application of accepted methods of management have been excellent.

CONDITIONS ON ARRIVAL AT YOKOSUKA

A thorough physical examination, chest x-ray, and routine laboratory examinations were made on all casualties arriving at Yokosuka. The results of these examinations were critically analyzed and used in classifying the patients' general conditions into three groups: fair, poor, and critical. A patient with a moderate hemothorax, some shortness of breath, no marked cardiorespiratory distress and the overall condition fairly well stabilized was classified as fair; if he had marked hemothorax, shifting mediastinum, moderate to severe respiratory distress, and a moderate to marked anemia, he was classified as poor; and if he had a combined thoracoabdominal injury, empyema, marked mediastinal shifting and dyspnea, peritonitis, wound evisceration and evidence of severe blood and electrolytic depletion, he was classified as critical. There were 248 fair, 132 poor, and 25 critical patients in this series. Infections were present in 25 instances as indicated in Table II.

TABLE II.—INFECTION

Type of infection	No. of cases
Empyema	16
With subphrenic abscess	1
With bronchopleural fistula	1
With gastrodiaphragmatic pleural fistula	1
With liver abscess	2
With biliary diaphragmatic pleural fistula	1
With tracheoesophageal fistula	1
Pelvic abscess	1
Lung abscess	1
	25

Different types of traumatic chest lesions at the time of admission are listed in Tables III, IV, V, and VI.

The majority of patients in this series were involved in two campaigns: the amphibious landing at Inchon followed by the advance to Seoul in September and October 1950, and the withdrawal after the intervention of the Chinese Communists in November and December 1950. In both instances unstable and unfavorable tactical conditions resulted. Under such circumstances there was steady pressure exerted upon the forward medical facilities by the constant receipt of casualties. This, of course, resulted in too early evacuation, contrary to ideal surgical management of the individual. The pressure exerted upon the forward areas was such that many casualties arrived in Yokosuka without having received adequate initial resuscitative measures and needed surgery. Many others were evacuated from the forward area immediately following major surgical procedures too soon for their condition to have become stabilized, arriving in a very precarious condition. With large numbers of casualties arriving in such poor condition, it might be expected that mortality would be higher. Fortunately, our mortality rate did not approach our expectations. In large measure, the excellent results were owing to unselfish devotion to duty and many long hours of labor and effort on the part of the medical officers, nurses, and hospital corpsmen who cared for these casualties.

TREATMENT INSTITUTED IN YOKOSUKA

The resuscitative therapy. Since many of the patients arrived in poor and critical condition, resuscitative measures were mandatory before any definitive surgery could be instituted. The immediate correction of the cardiorespiratory imbalance was the most important single factor in aiding them. These measures were carried out according to the degree of the abnormal condition present. For the most part, fluid replacement was limited to blood, and every effort was made to replace the amount of blood lost by volume for volume at least. Undoubtedly, the routine use of antibiotic therapy at the forward medical facilities was an important factor in reducing the incidence of infection. We used penicillin routinely and streptomycin as indicated on all patients coming to our care until the pleural cavity was cleared and the lungs completely re-expanded. The practice of instilling penicillin and streptomycin locally into the pleural cavity, as carried out by others, was not found to be essential by us. We practiced doing it at the beginning but soon abandoned the procedure when

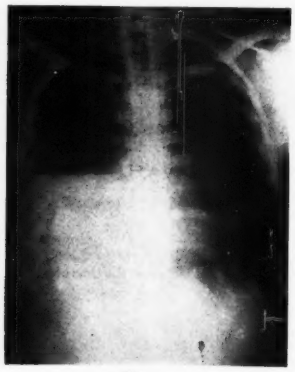

Fig. 1.

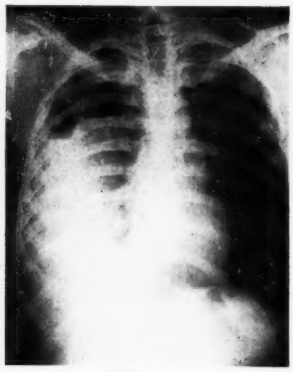

Fig. 2.

Fig. 3.

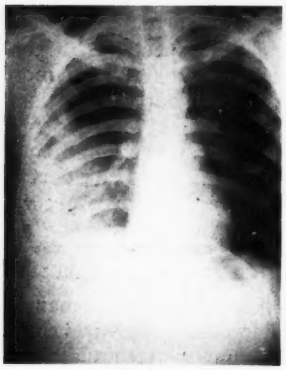

Fig. 4.

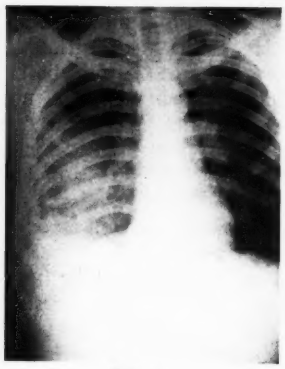

Fig. 5.

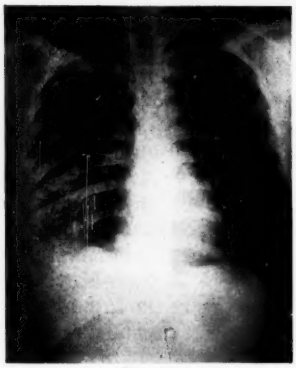

Fig. 6.

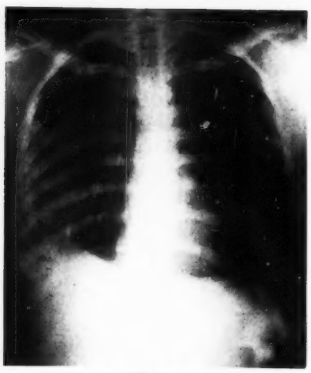

Fig. 7.

Fig. 1. Case 1. Roentgenogram of the chest showing a marked hemopneumothorax in the right side and a completely collapsed lung.

Fig. 2. Case 1. Roentgenogram of the chest after 2 weeks showing fluid and air decreasing in amount and the lung re-expanding.

Fig. 3. Case 1. Roentgenogram of the chest after 4 weeks showing the fluid and air to be further decreasing and the lung re-expanding.

Fig. 4. Case 1. Roentgenogram of the chest after 6 weeks showing further reduction in fluid and air content and a continual lung re-expansion.

Fig. 5. Case 1. Roentgenogram of the chest after 8 weeks showing a continuous clearing of the pleural cavity and further lung re-expansion.

Fig. 6. Case 1. Roentgenogram of the chest after 10 weeks showing the pleural cavity cleared of fluid and air and the lung continuously re-expanding.

Fig. 7. Case 1. Roentgenogram of the chest after 12 weeks showing the lung completely re-expanded.

it appeared to make very little difference in the ultimate recovery of the patient.

Hemothorax. Hemothorax accounted for over 66 per cent of the traumatic thoracic surgery series, and its management is of prime importance. From the beginning we accepted the principle of early re-expansion of lung and vigorously applied this principle to the fullest

extent. Persistence and patience are watchwords. We had no hesitation in repeating as many aspirations as necessary until the pleural space was dry; for instance, in Case 1 a total of 60 aspirations were done. Aspiration of the chest was begun at once, if necessary; then repeated at least once daily. The progress resulting from daily aspiration was followed by weekly x-ray examination of the chest. All patients were encouraged to practice breathing exercises every hour daily, while in the hospital (Table VII).

CASE 1. Hospital No. 24284. A 20 year old marine sustained a gunshot wound in his right chest on August 12, 1951. Examination at the forward medical company revealed the wound of entrance 2 inches below the right nipple and the exit at the inferior angle of the right scapula. The wound was sucking; marked dyspnea and evidence of shifting mediastinum were noted. Penicillin and streptomycin were administered, and oxygen therapy was instituted. The sucking wound was closed. On the next day a thoracentesis was done and "a large amount of blood was withdrawn." He was transferred to a hospital ship where 4 more thoracenteses were done. No record of the amount of fluid withdrawn was noted but he did receive several blood transfusions before he arrived at Yokosuka on August 27, 1951. On admission, at Yokosuka, his general condition was poor, and he had moderate dyspnea, definite sagging of the right shoulder, and a moderately contracted right chest. X-ray examination of the chest revealed a marked hemopneumothorax with a slight shifting of the mediastinum (Fig. 1). While in this hospital, antibiotic therapy was continued, 2 blood transfusions of 500 cubic centimeters were given, and daily thoracentesis was done. A total of 60 aspirations were done from August 28 to October 26 and the amount of fluid withdrawn, each time, varied from 20 to 300 cubic centimeters. On August 31, the fluid withdrawn appeared slightly purulent. A culture was taken and later reported positive for nonhemolytic streptococcus. From August 31 to September 10, the pleural cavity was irrigated at each aspiration with 50 cubic centimeters of 0.5 per cent acetic acid and 15 per cent glycerin in normal saline solution. The subsequent chest fluid withdrawn became culture negative. While daily chest aspiration was carried out, a weekly follow-up x-ray examination of the chest revealed steady progress of lung re-expansion (Figs. 1 to 7). He ran a low grade temperature of 100 degrees F. from August 27 to September 11. His contracted chest was gradually restored to normal and x-ray examination of the chest just prior to his discharge revealed more than 95 per cent lung re-expansion. He was discharged to duty on November 21, 1951 in excellent condition.

TABLE III.—CHEST LESIONS

Type of lesions	No. of cases
Hemothorax	
Minimum	37
Minimum with aneurysm axillary artery	1
Moderate	110
Moderate complicated with biliary fistula	3
Moderate clotted	10
Marked with shifting mediastinum	29
Marked bilateral	3
Total	193
Pneumohemothorax	13
With sucking chest wound	5
With shifting mediastinum	3
With subcutaneous emphysema	9
Total	30
Empyema (See Table II)	23
Pulmonary hematoma	10
Perforating wounds, lung re-expanded, minimum or no fluid	66
Perforating wounds, with incomplete lung re-expansion	7
Pneumothorax	3
Tension pneumothorax	2

TABLE IV.—ORGANS INJURED IN 54 COMBINED THORACOABDOMINAL WOUNDS

Organs injured	No.
Diaphragm	34
Liver	21
Spleen	9
Kidney	9
Ureter	1
Stomach	8
Small intestine	5
Large intestine	6
Shell fragments in retroperitoneal region	2

This patient certainly was a candidate for pulmonary decortication, but it illustrates how this major surgical procedure can be completely eliminated by patience and persistence in aspirating the chest. It also illustrates how a full developing empyema can be aborted by the use of acetic acid, glycerin, and normal saline solution irrigation at each aspiration.

At the outset of World War II there were three schools of thought: (1) energetic aspira-

TABLE V.—CARDIAC AND MEDIASTINAL WOUNDS

Type of lesions	No. of cases
Hemopericardium	2
Shell fragments in pericardial sac	2
Shell fragments in cardiac ventricle with hemopericardium	1
Shell fragments in mediastinum	7
Tracheoesophageal fistula (gunshot wound)	1
Laceration, descending thoracic aorta	2
	15

TABLE VI.—FOREIGN BODIES
(FRAGMENT OR BULLET)

Locations	No. of cases
Lungs	43
Chest wall	34
Mediastinum	7
Cardiac ventricle	1
Pericardial sac	2
Retroperitoneal region	2
	89

tion repeated often enough to keep the chest dry; (2) watchful waiting in which aspiration is performed only to relieve cardiorespiratory embarrassment; and (3) a line of treatment that is somewhat midway between the two, consisting of aspiration and of partial replacement with air. Since experience gained in World War II, the conservative regimen has for the most part been abandoned and advocates of early and repeated thoracentesis without air replacement appear to be in the majority. It is believed that the basis of treatment of all intrathoracic wounds lies in an attempt to secure total expansion of the lungs at the earliest possible moment. A hemothorax is a foreign body situated in a most vital serous cavity; there is no means of predicting in which cases the blood will ultimately be absorbed by natural processes; and a hemothorax may cause infection any time from the moment it is produced until the time it is removed. The blood is purposely left in the pleural cavity by some surgeons who contend that its presence produces hemostasis by reason of the pressure which the mass of fluid exerts upon the damaged lung. This conception is based upon several false assumptions. First, it is only likely to have any effect if the bleeding happens to come from the lung, and continued bleeding is almost certainly not of pulmonary origin; second, unless the wound happens to be at the bottom of the lung, the level of compression blood might have to rise to the top of the chest before it can staunch the flow; third, bleeding either into a serous cavity or into the intramuscular planes is more likely to continue into a hematoma than if that blood be cleared out. Finally, aspiration might start fresh bleeding if it carries a too high negative pleural pressure. Our observations have found that this is not the case and that it is the exception for bleeding to recur following aspiration. Moreover, bleeding from any intercostal or internal mammary artery cannot be prevented by allowing blood to remain in the pleural cavity.

TABLE VII.—THORACENTESIS

No. of patients	250
No. of thoracenteses performed	1,843
Average No. thoracenteses performed in each patient	7.3
Largest No. thoracenteses performed in 1 patient.	60
Total amount of fluid removed, c.c.	201,000
Average amount of fluid removed in 1 patient, c.c.	820

The only x-ray examinations of any diagnostic value are those made with the patient in a sitting position. Extrapleural hematoma is not uncommon—this condition is generally mistaken for a hemothorax. Hemothorax may be indistinguishable, clinically, from atelectasis, and this is particularly true if the clot has been deposited at the bottom of the pleural cavity. There is no definite way of assessing how much blood is present in the pleural cavity in any given instance. It is generally reliable to assume that a great deal more fluid is present than one expects. The earliest signs of a large hemothorax are shock, pain, and dyspnea. Hemothorax may exist, however, without any of these. Most patients with chest wounds are frightened at first, and often they either "struggle for breath" or indulge in rapid respiration, both of which militate against efficient breathing.

To be really effective, aspirations should be started within 24 hours after the patient has been wounded. If conditions in the forward area are such that this is impracticable, treatment should be started as soon as possible afterward. A delay of 5 to 6 days greatly increases the difficulties of drying the pleural cavity. An efficient management of a hemothorax demands early, persistent, and repeated aspirations of the pleural cavity. Air replacement should not be done. We have found that aspirations of the pleural cavity are often done too low, just as pleural drainage is likely to be too high. When aspirations cease to yield a ready flow of blood it is generally said that clotting has occurred. This may be a convenient explanation but it often bears but little connection with the actual condition of the pleural cavity.

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 8. Case 2. Roentgenogram of the chest on admission, showing a marked hemothorax in the right side and a moderate shifting of the mediastinum.

Fig. 9. Case 2. Roentgenogram of the chest 1 week after decortication, showing clearing of the pleural cavity and re-expanding of the lung.

Fig. 10. Case 2. Roentgenogram of the chest, 2 months after decortication, showing the lung satisfactorily re-expanded.

Fig. 11. Case 2. Photograph at the time of discharge of the patient from the hospital showing the wound of the bullet entrance just above the anterior third of the thoracotomy incision.

Fig. 11.

Massive clot is a definite entity but is comparatively rare, whereas difficulty in aspirating the blood is common. It is generally due to faulty selection of the correct site, e.g., when aspiration is made too low, or to the presence of isolated clots, fibrin, and loculation. Our experience revealed that it is quite usual to find several pints of fluid blood in the chest of a patient who is said to have clotted hemothorax. Aspiration should be high in the chest. The lowest level should be the ninth interspace in the posterior axillary line and the seventh interspace in the midaxillary line. (We have abandoned aspirating through the anterior side of the chest because more satisfactory results from aspirating through the posterior chest have been obtained.) The rationale for this concept is that the diaphragm is frequently elevated in hemothorax and most of the fluid portion is in the upper parts.

In most of these patients, the bleeding had stopped soon after the injury was sustained, and they responded rapidly to a few simple aspirations, as demonstrated by serial x-ray examination. In some instances bleeding continued slowly but persistently for days or weeks. Generally, the patients who reacted in this manner were those with injuries of the ribs and the chest wall. Thoracotomy is indicated as soon as this condition is diagnosed. In the few patients who may still be bleeding

TABLE VIII.—MAJOR OPERATIONS PERFORMED

Operations	No. of cases
Thoracotomy	
For drainage of empyema	15
Decortication of clotted hemothorax	3
Decortication of empyema	2
For removal of foreign bodies from lung	10
For removal of foreign bodies from pericardium	1
Pulmonary hemorrhage	2
Laparotomy	
For gastric hemorrhage	1
For repair of wound dehiscence	1
For intestinal obstruction	1
Laminectomy for transection of spinal cord	6
Ligation of aneurysm, right axillary artery	1
Ligation of aneurysm, right radial artery	1

profusely, an adequate blood transfusion should be given, and the bleeding point should be secured by thoracotomy as soon as possible.

The importance of remedial breathing exercises in the management of chest injury cannot be overemphasized. Many patients came to us with marked body deformity and reduced pulmonary function because they had neglected this important physical therapy. It should be emphasized that this misfortune can be reduced to a negligible figure if the remedial breathing exercise is instituted early, persistently, and frequently.

The unfortunate sequelae of inadequately treated hemothorax are: (1) empyema; (2) reduced pulmonary function; (3) late pulmonary suppuration; and (4) body deformity.

Clotted hemothorax. Clotting has been reported to be about 10 per cent. The treatment of clotted hemothorax passed through interesting phases during World War II, from the conservative measure of allowing natural absorption to simple evacuation of clot and finally evacuation of clot with decortication. Small clotted hemothoraces may be absorbed or organized to such a degree that little residual disability remains, but more commonly there is considerable fibrous tissue formation, often with calcification or ossification later leading to a deformed and immobile or "frozen chest." Simple evacuation of the clot was the first active operative measure undertaken in an attempt to overcome the disability of the frozen chest. Success was achieved in some early patients. But, in many, the lung failed to re-expand fully, and a residual pleural pocket remained which gradually was obliterated by fibrous tissue leaving the crippling deformity of the frozen chest. It became obvious after a little experience with simple evacuation that decortication or removal of the fibrous tissue layer on the visceral pleura was required to permit the underlying lung to re-expand completely and obliterate the pleural space (Case 2).

CASE 2. Hospital No. 21546. A 21 year old marine sustained a gunshot wound of his right chest June 11, 1951. He had had 3 thoracenteses in forward areas with removal of several hundred cubic centimeters of blood prior to evacuation. He arrived at Yokosuka on June 17, 1951. At the time of admission, his general condition was poor, and he had moderate dyspnea and some paradoxical breathing due to a frail chest wall resulting from several fractured ribs on the right side. The x-ray examination of the chest revealed a marked hemothorax with some shifting of the mediastinum (Fig. 8). Aspiration was done 6 times, and 2,000 cubic centimeters of blood were withdrawn. Since follow-up chest x-ray films revealed no evidence of progress in re-expanding the lung and large amounts of fresh blood continued to be withdrawn, it was suspected that there was a large hematoma in the pleural cavity and that bleeding continued into the hematoma. On June 29, an exploratory thoracotomy was done and a large hematoma with a clot was found. The lung was completely collapsed and encapsulated by a moderately thick layer of fibrous tissue. Following evacuation of the clot and complete hemostasis, decortication was carried out, and the lung was freed and re-expanded. The postoperative course was uneventful. He was discharged August 8, 1951 in excellent condition (Figs. 9 to 11).

There were 10 cases of so-called clotted hemothorax, an incidence of 2.4 per cent. All these cases developed prior to arrival at this hospital. Our efforts in carrying out the chest aspirations were so persistent, no opportunity was left for any patient to develop a clotted hemothorax, once he was in our care. Moreover, in those who already had developed this type of complication on admission, we were able to clear the pleural cavity and re-expand the lung in 50 per cent of the patients. On the basis of this experience, it may be stated that by this simple procedure alone it is possible to reduce, if not to eliminate almost completely, the number of decortications to a negligible number. Therefore, a special plea is made for early, persistent, and frequent aspiration in the management of hemothorax (Case 1).

Pneumothorax. There were 2 instances of tension pneumothorax among the 35 patients with pneumothoraces and pneumohemothoraces (Table IX). Basically, the management for this type of chest lesion is the same as that for hemothorax, and under this regimen of treatment every patient in this series responded satisfactorily. The chest cavity became free of air and fluid, and the lung completely re-expanded. We did not find it necessary, in any instance, to introduce an intercostal catheter into the pleural cavity to withdraw air.

Hematoma of the lung. This form of lesion may result from wounds of the lung or from contusion without pleural penetration. A total of 10 patients are considered in this series. No surgical interference was required in management. As a rule they cleared almost completely in from 1 to 4 weeks.

Cardiac and mediastinal injury. It is difficult to estimate the incidence of this type of war injury because undoubtedly most of these wounds were immediately fatal, since the use of a tourniquet or pressure control was not possible in most of these vascular injuries. However, a few patients reached a base hospital after travelling a great distance for definitive treatment. The hemorrhage was at least temporarily controlled by certain limiting anatomic structure and by the hematoma and infiltration of the surrounding muscles and tissues.

Of 14 patients with cardiac and mediastinal injuries, 2 with hemopericardium were treated with pericardicentesis and improved. In 2 patients shell fragments in the pericardial sac were removed. One patient with shell fragments imbedded in the cardiac muscle, without symptoms, was evacuated. Six patients with shell fragments in the mediastinum were managed conservatively since the fragments were small in size and asymptomatic. Two patients died from rupture of the descending aorta involving a previous lacerated wound that apparently had been temporarily sealed off, and one with a tracheoesophageal fistula died of aspirated pneumonia, empyema, and mediastinitis.

Foreign bodies in the chest. The removal of metallic foreign bodies from the lung did not present much of a problem. The simplicity of the procedure and the excellent results obtained in this series suggest the routine removal of the large foreign bodies from the lung. The minimum size for removal was decided to be 1 by 2 centimeters. In general, it was our policy to individualize each instance, and in deciding on its removal, the following factors were taken into consideration: (1) size and position of the foreign body; (2) signs and symptoms produced by it; and (3) the psychosomatic effects upon the patient aware that he had a piece of metal in his lung.

TABLE IX.—PNEUMOTHORAX

Type of lesions	No. of cases
Pneumohemothorax	13
With sucking chest wound	5
With shifting mediastinum	3
With subcutaneous emphysema	9
Pneumothorax	3
Tension	2
	35

TABLE X.—FOREIGN BODIES

Location	No. of cases
Lung	43
Chest wall	34
Mediastinum	7
Myocardium	1
Pericardial cavity	2
Retroperitoneal space	1
	88

Forty-three patients, or 10.6 per cent in the series, were found to have a metallic foreign body in the lung (Table X). Thoracotomy was performed for removal of a foreign body in 11 patients. All 11 patients recovered from the operation and returned to duty. Since this type of surgery is an elective procedure the patient generally is allowed to recover from his wound as completely as possible before being subjected to surgical removal.

Empyema. Infection with the resulting empyema was a grave problem in World War I and to a lesser extent in World War II. The incidence varied from 25 to 30 per cent. It accounted for a considerable part of the high death rate and morbidity. Empyema was observed in 39 patients (9.6 per cent) in this series. Undoubtedly, the early and routine use of antibiotic therapy played an important part in lowering the incidence of infection.

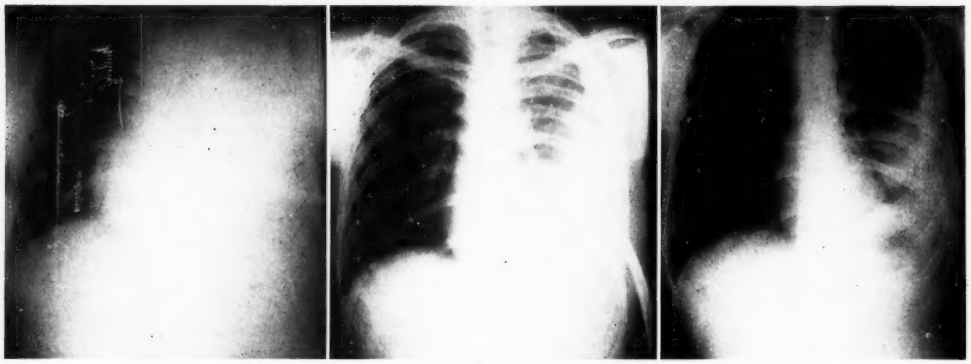

Fig. 12. Fig. 13. Fig. 14.

Fig. 12. Case 3. Roentgenogram of the chest, at the time of admission, showing a marked hydrothorax with a moderate shifting of the mediastinum.

Fig. 13. Case 3. Roentgenogram of the chest, 1 week after open thoracotomy tube drainage, showing clearing of the left pleural cavity and re-expanding of the lung.

Fig. 14. Case 3. Roentgenogram of the chest, 2 weeks after open drainage of the empyema, showing the pleural cavity cleared of fluid and the lung satisfactorily re-expanded.

However, while it is believed to be an important adjunct, we did not accept antibiotic therapy as a substitute for adequate initial excision of devitalized tissue. Basically, the treatment of empyema is the same as that of hemothorax, that is, rapid clearing of the pleural cavity and early and complete re-expansion of the lung.

Of 39 patients with empyema, 2 required pulmonary decortication; 12 were treated by thoracotomy with catheter drainage and irrigation with a solution of 0.5 per cent acetic acid, 15 per cent glycerin in normal saline. Twenty patients responded to daily aspiration and irrigation and 5 deaths resulted from complications. We have used this acetic acid-glycerin-normal saline solution as a wet dressing for contaminated and dirty wounds with excellent results. (It is better than any other agent now available for local application, because it controls infection, cleans the wound, stimulates tissue healing, deodorizes the wound discharge, requires little or no frequency in change of dressing and it is simple to apply.) We found its use in irrigation of empyema equally effective (Case 3).

Lung injury. There were 4 lobectomies and all were done prior to admission, 1 on the right middle lobe and the others on right lower lobe. In analyzing the clinical records of these 4 patients, it was noted that all were operated on for hemothoraces, and the resections were carried out for lacerated wounds of the lung. There was no record as to the extent of the laceration of the lung. In all of these patients intercostal drainage tubes were used and all developed empyema postoperatively. On the basis of the available information, these radical procedures could have been avoided. The lung has remarkable ability to heal, and for this reason the lacerated lung, which may appear hopelessly damaged, in a few weeks usually will be restored almost to normal without resection.

Thoracoabdominal wounds. Intra-abdominal hollow viscus perforation or injury of a solid organ such as the liver or spleen in association with intrathoracic injury makes immediate surgical intervention mandatory. The associated abdominal wound is especially dangerous because of the likelihood of bacterial contamination both of the peritoneum and pleura. Shock usually is more marked in thoracoabdominal injuries than in thoracic injuries alone (Case 3). The mortality, therefore, has been very high—33.8 per cent reported in World War II. All patients coming to us from the forward areas in critical condition had suffered this form of injury.

Tables I and IV reveal that only 1 thoracotomy and 3 combined thoracoabdominal explorations were performed in 54 patients

having thoracoabdominal wounds, and of the total 46 laparotomies that were done 43 were performed in the forward medical facilities. There are two factors which appear to have influenced the choice of surgical management in the forward areas. First, because of the tactical situation, heavy pressure was exerted to evacuate the casualties too soon; under such circumstances there was little or no opportunity for a careful study and observation of intrathoracic injury. In many instances they were overlooked. The second factor was that among the medical personnel in the forward medical facility there were no trained thoracic surgical teams.

CASE 3. Hospital No. 20419. A 23 year old marine was struck by a mortar shell on May 28, 1951 and sustained a fragment wound on the left side. At a forward medical company a laparotomy was performed and a laceration of the stomach was repaired. He was evacuated immediately following the operation and on June 2 arrived at Yokosuka in a very poor condition. He was in acute respiratory distress with cyanosis and rapid pulse. X-ray examination of the chest revealed marked hydrothorax with moderate shifting of the mediastinum (Fig. 12). Immediate thoracentesis was carried out to relieve the respiratory distress and to restore the cardiorespiratory imbalance. A total of 8 aspirations were done and 2,700 cubic centimeters of purulent, sanguineous fluid were withdrawn. On the sixth day after his admission, when his condition was well stabilized, a rib resection was done for drainage of empyema. The left pleural cavity was found to contain digested gastric content in addition to pus. Daily irrigation with acetic acid-glycerin-normal saline solution was instituted and the pleural cavity was connected with a suction. The discharge from the pleural cavity gradually became clear serous in character, accompanied by slow but steady lung re-expansion (Figs. 13 to 14). The intercostal tube was removed on the thirteenth day. His condition improved rapidly, and on July 14 he was evacuated to the United States for subsequent convalescence. The last report received from the patient 5 months following his return from the overseas hospital revealed that his convalescence had been uneventful. The lung re-expanded and he later returned to duty.

RESULTS OF TREATMENT

Lung re-expansion. Since the objective in treatment of thoracic injuries is to obtain early lung re-expansion, a frequent x-ray follow-up study was made in every patient under treatment. No treatment was considered completed without full re-expansion of the lung.

TABLE XI.—LUNG RE-EXPANSION

Re-expansion percentage	No. of cases
Full	340
70–95	44
50–70	8
30 or less	5

As indicated in Table XI, 340 patients (85.6 per cent) regained full lung re-expansion; in 52 patients (13 per cent) lung re-expansion varied from 50 to 95 per cent. It was our impression that full re-expansion would eventually occur in this latter group, and that no other surgical measures would be required. Only 5 patients (1.2 per cent) who required decortication failed to regain less than 30 per cent re-expansion.

Complications. Of the 16 patients who developed empyema while in this hospital, 11 were previously treated with closed thoracotomy catheter drainage for hemothorax. Our own experience indicated not only that a higher incidence of infection resulted from the use of the thoracotomy tube, but that should thoracentesis be necessary after removal of the tube, it was more difficult because of fluid loculation resulting from adhesions produced by the tube. Moreover, use of closed drainage for hemothorax quickly lost its effectiveness within 48 hours owing to occlusion of the tube by fibrin and clots and by pleural adhesions about the intrathoracic portion of the tube. Finally, use of the thoracotomy tube with underwater drainage required more attention and expert care, especially in transit. It should be emphasized that there is no good reason for using a procedure in treatment which tends to increase morbidity and at the same time contributes to no better results than sim-

TABLE XII.—COMPLICATIONS

Type of complication	No. of cases
Empyema	16
Intrathoracic bleeding	
Empyema	3
From descending aorta	2
From intercostal artery	1
Kidney bleeding	2
Subphrenic abscess	2
Aneurysm, innominate and subclavian arteries	1
Hematemesis	1
Pulmonary embolism	1
Intestinal obstruction	1
	30

ple needle aspiration, a procedure which is safer and more effective, as we have already demonstrated.

STREPTOKINASE AND STREPTODORNASE

The use of streptokinase and streptodornase in the treatment of hemothorax has been a favorite subject in recent medical literature. We used it only in 2 instances. It was for two obvious reasons that we did not use it as extensively as might be expected. In the first place, it was not available to us at the outset of the Korean War, and, secondly, we had found our method of treatment so effective that further treatment was not required. It was available to us toward the end of our overseas duty, and we used it in 2 instances of hemothorax which developed into empyema and resulted in a nonexpanded lung. The result from its use in these cases was excellent. However, it must be stated that we have not used this agent often enough to enable us to make a critical evaluation of it.

MORTALITY

There are many obvious difficulties in determining the number of deaths from chest wounds. An estimate that chest wounds are involved in from one-third to one-half of the total killed probably is not far from accurate. Our observation on the admission of casualties to this hospital revealed that thoracic casualties outnumbered the abdominal casualties at least 2 to 1. Sauerbruch in 1914 counted 300 dead soldiers on a battlefield and found that 122 (37 per cent) had gunshot wounds of the chest. Because many casualties came to us either without receiving adequate resuscitative measures after injury or too soon following major surgical procedures, we had to assume the additional function of a forward hospital. Therefore, it might be expected that our mortality rate would be higher than the mortality rate of a similar institution which was located in the rear and functioning only as a base hospital.

In reviewing the literature on the number of deaths among the wounded brought in for treatment, we found an extraordinary difference in statistics:[1]

[1]These figures refer to penetrating and perforating wounds.

	Per cent
English in the Crimea War	79.2
American Civil War	62.6
Franco-Prussian War (German)	56.7
Spanish-American War (U.S.)	24.5
Boer War (British)	14.0
World War I (British)	27.0
Sino-Japanese War 1937 (Chinese)	14.8
World War II	8.1
Tokyo Army Hospital 1950 to 1952	0.6

The total mortality in this series, regardless of the associated injuries or diseases, was 1.9 per cent. In a total of 8 deaths, only 5 (or about 1 per cent) could be attributed to the chest wound alone. The remaining deaths were accounted for by accompanying severe abdominal wounds in 2 and by pulmonary embolism from thrombosis of pelvic veins in 1.

FINAL DISPOSITION OF THE PATIENTS

Our action on the disposition of patients was induced, generally, by the overall evacuation policy prescribed for the casualties. This policy implies that any patient who, in our judgment, requires more than 90 days of hospitalization before being returned to duty is to be evacuated to the Continental United States.

There were 318 patients (80.1 per cent) who recovered and were fit for duty within 90 days. Among these, 79 had accompanying injuries and had to be transferred to other services for treatment and disposition. Only 81 (20 per cent) were evacuated to the United States because of chest injury.

SUMMARY

A brief review has been presented of the basic problems involved in the evacuation and management of thoracic casualties of Navy and Marine Corps from Korea. The tactical situation, the mountainous terrain, and adverse climatic conditions were important factors that determined the practice in the care and the evacuation of casualties.

Evacuation from the forward areas, most frequently, was carried out under pressure, and in most instances the evacuation was accomplished too early following major surgery and too soon following major trauma without the benefit of adequate resuscitative measures.

The basic principles learned in World War II were applied in the management of chest injuries: (1) conservative initial management; (2) early and complete re-expansion of the lung; and (3) remedial breathing exercises.

The age of the patients in this study ranged from 18 to 36 years, the average age being 20 years. The average time interval from battlefield to arrival at Yokosuka was 7 days; the shortest time interval was less than 24 hours; however, over 50 per cent of the patients arrived within 3 days.

Among 405 chest wounds, 219 were from small arms; 169 from shell fragments; 16 from contusion; and 1 from blast effect. Thoracentesis was accomplished in 124 patients in forward medical facilities; an average of 2.8 per cent aspirations were made and 939 cubic centimeters of blood were withdrawn in each instance. A total of 53 thoracotomies, 3 thoracoabdominal explorations, and 43 laparotomies were performed in forward areas. Among 53 thoracotomies, there were 4 decortications, 4 lobectomies, and 33 thoracotomy tube drainages.

Condition on arrival was: fair in 248 cases, poor in 132 cases, and critical in 25 cases. Infection was present in 39 cases, or 9.6 per cent. Hemothorax was present in 66.6 per cent. In each patient with a hemothorax an average of 7 thoracenteses were performed in the hospital. The major surgical procedures performed were listed.

The problems concerning the management of hemothorax have been discussed. Efficient management demands early, persistent, and repeated aspirations accompanied by remedial breathing exercises. Air replacement was not done. The use of thoracotomy tube drainage for treatment of hemothorax resulted in a high incidence of complications.

In 10 patients (2.4 per cent) clotted hemothorax was noted, and in half of these the condition was cleared by intensive aspiration. Decortication was done on the remaining patients. All cases of clotted hemothorax and unexpanded lung resulted from inadequate treatment or mismanagement.

The management of empyema with the use of an acetic acid-glycerin-normal saline solution as a local irrigating agent was discussed, and the effectiveness of this solution in clearing up the empyema was emphasized.

The management of pneumothorax, hematoma of lung, cardiomediastinal injury, foreign bodies in the chest, thoracoabdominal wounds, and lung laceration was discussed.

The results of treatment by lung re-expansion indicated full re-expansion in 85.6 per cent; in 13 per cent 50 to 95 per cent re-expansion; and in only 1.2 per cent, less than 30 per cent re-expansion that required decortication.

Infection and hemorrhage accounted for the majority of complications, and the use of closed thoracotomy tube drainage for the treatment of hemothorax was found to be an important contributory factor in the high morbidity rate.

The total mortality in this study, regardless of the associated injuries or diseases, was 1.9 per cent. Only in 5 instances, or about 1 per cent, could death be attributed to chest wounds.

A total of 317 patients, or 80.1 per cent, had completely recovered and were fit for duty within 90 days. Eighty, or 20 per cent, were evacuated to the United States because of chest wounds.

CONCLUSIONS

1. Observation on casualties from the forward areas, especially, those evacuated too soon because of prevailing tactical situations indicates that, in general, conservative measures should be carried out initially.

2. The indications for an emergency thoracotomy are: continuing, rapidly accumulating, intrathoracic hemorrhage despite repeated thoracentesis; thoracoabdominal injuries; evidence of damage to the mediastinal viscera (esophagus, trachea, or large bronchus) causing pressure pneumothorax and certain cardiac injuries.

3. An efficient management of hemothorax demands early, persistent, and repeated aspiration accompanied by remedial breathing exercises. Air replacement following aspiration and the use of closed thoracotomy tube drainage should be avoided.

4. In general, clotted hemothorax and nonexpanded lungs result from inadequate treatment and mismanagement and could be pre-

vented. Pulmonary decortication, therefore, rarely should be a necessary procedure in the management of hemothorax.

5. The acetic acid-glycerin-normal saline solution is a valuable agent in the management of localized infection. It is effective as an irrigating agent in clearing up empyema.

6. It is hoped that the experiences which we have enumerated in this article, resulting from another tragic conflict which has already inflicted much suffering and loss of life, will be a helpful guide for both military and civilian surgeons in the treatment of future chest injuries.

THE COLLATERAL VENOUS DRAINAGE FROM THE KIDNEY FOLLOWING OCCLUSION OF THE RENAL VEIN IN THE DOG

W. HENRY HOLLINSHEAD, Ph.D., and JOHN A. McFARLANE, M.D.,
Rochester, Minnesota

HYPERNEPHROMAS of the kidney rather frequently produce obstruction of the renal vein, as observed by McDonald and Priestley, and at operation or necropsy it is usual to find greatly dilated veins in the perirenal fat. The anatomy of the channels developed as a result of obstruction by this malignant tumor, which invades the veins massively and tends to spread through them rather than through the lymphatics, has apparently not been described, and little is therefore known about their connections. The matter may be, however, of some clinical importance, for the rate of recurrence of such tumors after nephrectomy is relatively high, and a number of these recurrences are local ones; this suggests that extension of the primary growth into the enlarged perirenal veins and perhaps into the veins into which they empty may be a source of recurrence.

While it is recognized that the veins in the perirenal fat should be included in the resection when nephrectomy is done for hypernephroma, the lack of knowledge as to their connections raises the question as to whether it may be possible, by excising specifically some of the vessels into which they empty, to obtain a more nearly complete removal of the veins which are most likely to harbor tumor cells.

The present work was undertaken in order to determine experimentally what collateral venous channels are enlarged as a consequence of obstruction of the renal vein itself, and into what vessels they empty. The results indicate that in the dog, as is apparently true also in man, the normally delicate veins in the perirenal fat become grossly dilated, in consequence of their connections with the subcapsular (stellate) veins of the kidney, to provide a large part of the collateral circulation from the kidney. In the present experiments the ureteric veins likewise shared in this enlargement. The connections of these veins, although multiple and diverse, are in general with larger veins in the vicinity of the kidney, including the renal vein itself, the adrenal vein, the gonadal vein, and neighboring lumbar veins.

From the Section of Anatomy, Mayo Clinic and Mayo Foundation and the Department of Urology, Mayo Foundation.

The experiments and observations reported here form a part of Dr. McFarlane's work in the preparation of a thesis for the degree of Master of Science, the work being suggested by Dr. J. R. McDonald, Division of Surgical Pathology.

MATERIAL AND METHODS

The experiments were carried out upon dogs; 6 were females and 2 were males. Gradual occlusion of the renal vein, simulating its occlusion through the growth of a tumor and thus allowing time for the development of collateral venous channels, was produced through the use of cellophane tear-tape; this was placed around the renal vein reasonably snugly, but not tightly enough to produce any visible constriction of the vein, and was tied in position over a hemostat. Cellophane tape, acting as an irritant, produces a fibrosis of the connective tissue, and it was such a fibrosis that gradually reduced the lumen of the vessel and eventually, as found at necropsy, obstructed it completely.

In order to vary the conditions of obstruction as much as possible, the right renal vein was occluded in 4 animals, the left in the other 4. For the same reason, in half the cases in each group the occluding tape was placed about the renal vein as close to the posterior (inferior) vena cava as possible, while in the others the tape was placed as close to the hilum of the kidney as possible.

The dogs were operated upon under proper surgical anesthesia and aseptic conditions. The renal veins were approached through a left or a right rectus incision. Fat surrounding the renal vein was cleared away only from the region about which it was desired to place the tape; after this had been tied in position around the vein and observed to see that it was not at that time constricting the vein, the abdominal wall was closed in layers. Neither immediate nor delayed ill-effects of the operation were apparent; there were no infections, the animals remained in good health, and at postmortem examination the kidneys and ureters appeared grossly normal.

The animals were killed by deep anesthesia and bleeding, 2 to 2½ months after operation. They were then arterially embalmed with a solution of alcohol, glycerin, and carbolic acid; following this, the posterior (inferior) vena cava was injected through its thoracic end with colored liquid latex. After the injection mass had hardened, fat was carefully dissected away from both kidneys of each animal, and the major veins in the neighborhood of the kidney were traced out. Results were recorded not only in the protocols but also through sketches and photographs.

OBSERVATIONS

Anatomy. No systematic study of the normal anatomy of the renal veins and the minute veins in the perirenal fat in the dog has been undertaken in our study, but observations made at necropsy indicate a close correspondence between these veins in the dog (Fig. 1) and those in man. There are also certain differences in respect to the larger veins which should be noted, although they would not for the most part alter the applicability of these observations to a similar condition in man.

In the dog, as in man, each renal vein is typically single, being formed by converging tributaries within or close to the hilum of the kidney, and the two veins empty at approximately the same level into the vena cava. Because of the caudal slant of both renal veins from the hila of the kidneys to the vena cava, the difference in length between the left and right renal veins, so pronounced in man, is not so obvious in the dog; the left renal vein is only a little longer than the right one. The right renal vein receives, as in man, neither the gonadal (internal spermatic or ovarian) nor the adrenal vein; the left renal vein of the dog receives the left gonadal vein, but not the left adrenal vein. In the dog the left adrenal vein empties separately into the vena cava a little above the entrance of the left renal vein.

Except for the gonadal vein on the left side, neither renal vein in the dog has any obvious communications with other veins. Although in man connections of the left renal vein with the azygos system, the ascending lumbar and one or more lumbar veins, and the vertebral venous plexus are common, as pointed out by Anson and co-workers, no such connections have been observed in the limited series of animals used in our experiments. Either they are not commonly present in the dog, or they were so minute that they were not visible; in any event, no collateral channels corresponding to these connections in man were found in the dog, either on the normal side or on that side on which the renal vein had been occluded. As in man, the renal veins receive one or two small ureteric veins running along the upper portion of the ureter, which usually enter the renal vein within the shelter of the hilum of the kidney. As the renal veins pass to the vena cava they also receive small venous twigs from the surrounding fat.

The other large veins in the region of the kidney are not unlike those of man. Note has already been made that both adrenal veins in the dog empty separately into the vena cava, and it might also be pointed out that these veins in the dog, as they enter the vena cava, actually represent adrenolumbar veins rather than adrenal veins alone (just as the left adrenal vein in man is usually joined by the left inferior phrenic), for a lumbar vein passes over the lateral and ventral surfaces of the adrenal gland to receive the blood from this gland. Also, because of the presence of the ovaries, fallopian tubes, and even most of the uterus in the abdomen rather than the pelvis proper, the ovarian vessels in the female dog are relatively much shorter than they

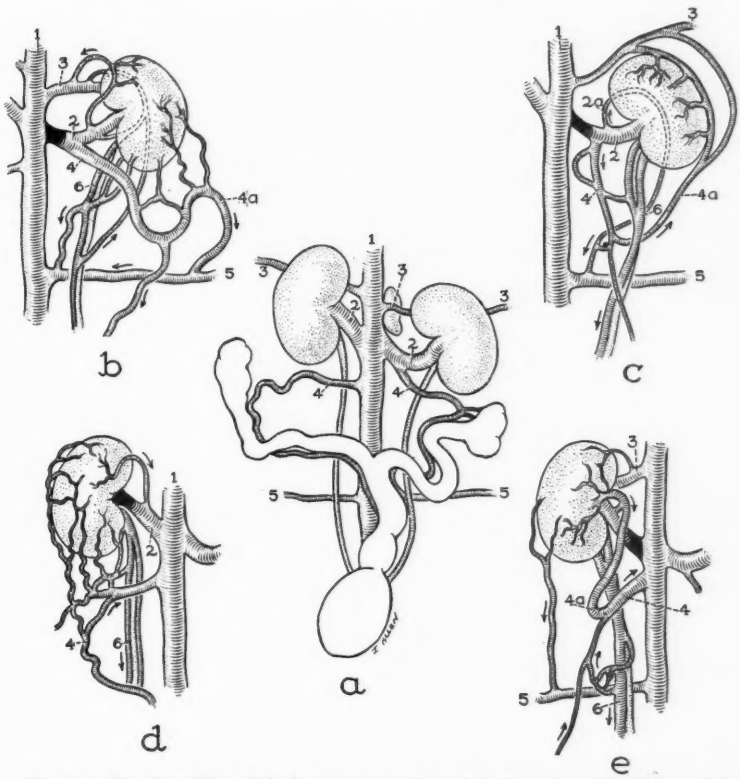

Fig. 1. a, The disposition of the larger venous channels in the region of the kidney of the dog, diagrammed as they appear in the female. The ureteric and other normally very small veins are not shown. *1* designates the posterior (inferior) vena cava, *2* the renal veins, *3* the adrenolumbar veins, *4* the ovarian veins, and *5* a pair of lumbar veins below the renal level. b, c, d, and e, Diagrams of the venous drainage of the kidney following occlusion of the renal vein. The level of the occlusion is indicated by the solid area of the vein; the arrows indicate the probable direction of blood flow in the veins. In b, the ovarian vein, *4*, is greatly enlarged proximally, and apparently was carrying a great deal of blood from the kidney; it has a prominent connection, *4a*, to a lumbar vein, *5*, but below the level at which this connection leaves, it is still somewhat enlarged. The ureteric veins, *6*, are also much increased in size, and have developed a large communication to the lumbar vein, but below this are still greatly enlarged. Both the ureteric vein and the ovarian vein and its connections receive capsular veins from the surface of the kidney. There are also enlarged anastomotic channels, behind the kidney, between the ureteric, renal, and adrenal veins, and a direct channel from the renal to the adrenal vein. In c, the chief drainage of the kidney is by way of the ureteric veins, *6*, and the adrenolumbar vein, *3*. The internal spermatic, *4*, also participates in its proximal part, but is not enlarged distally; it has a connection to the ureteric vein, and a small one to the lumbar, *5*, below the kidney, but primarily drains upward by *4a* into the adrenolumbar vein. The renal vein has a small connection, *2a*, to a lower lumbar vein. The capsular veins drain mostly into the arch, *4a*, along the convex border of the kidney, and hence into the adrenolumbar vein. In d, the patent portion of the renal, *2*, and the ovarian, *4*, receive capsular veins, and return blood from them directly to the vena cava; the ovarian is much enlarged proximally only. The ureteric veins, *6*, greatly enlarged throughout their lengths, assist materially in the venous drainage. There were no prominent connections to either the adrenolumbar or a lower lumbar vein. In e, capsular veins drain into the adrenolumbar, *3*, a lower lumbar, *5*, and the internal spermatic, *4*. The internal spermatic receives a very large capsular vein, *4a*, which itself receives a communication from the renal vein; it also receives a communication from the ureteric vein, *6*. The ureteric vein is very greatly enlarged.

are in the human female; as in the latter, however, they anastomose with the uterine vessels below. The adrenolumbar vein, sometimes other lumbar veins, and the ovarian or internal spermatic vein receive, like the renal vein, small and apparently variable twigs from the retroperitoneal fat.

In addition to the renal vein, the kidney of the dog, like that of man, has very tiny subcapsular or stellate veins, which, at least in well injected specimens, can be seen spreading between the true capsule of the kidney and the renal cortex. As in man, these are normally tributaries of the renal vein. Connecting with some of these subcapsular veins are exceedingly tiny veins which pierce the capsule of the kidney either to enter the fat around the kidney or to drain from this fat into the renal vessels. In the normal dog these vessels are so small that they could rarely be traced through the fat, but observations upon them when they were enlarged through renal venous obstruction indicate that they correspond closely in their anatomy to the veins of the fat about the kidney of man; they have been called "capsular" veins, apparently in reference to the fact that they drain the adipose capsule of the kidney. Through the capsular veins the subcapsular or stellate veins have diverse extrarenal connections, for the capsular veins communicate with the renal vein or some of its tributaries near the hilum of the kidney; with the adrenal vein, above; with the gonadal vein below; with lumbar veins; and with the ureteric veins. These connections correspond to those described by Tuffier and Lejars as existing in man.

The collateral venous drainage. The two sets of channels which invariably showed marked enlargement following occlusion of the renal vein, and this regardless of the point at which the vein was occluded, were the ureteric veins and the subcapsular-capsular vessels. It was the capsular veins and their connections, including those with the ureteric veins, that formed multiple tortuous channels in the perirenal fat, apparently entirely comparable to those seen in man when the renal vein is occluded by a hypernephroma.

As the ureter itself was not included in the fibrosing ligature, the connections of the ureteric veins with the renal vein at the hilum of the kidney were not occluded, and they, therefore, always formed a prominent part of the collateral circulation from the kidney in the experimental animals. The ureteric vein was usually doubled at its renal end, and sometimes this doubling extended throughout the length of the vein, though more commonly the two channels united at a variable distance below the lower pole of the kidney. It was only the renal ends of the ureteric veins that were always enormously enlarged; in the neighborhood of the kidney the ureteric vein or veins often received additional tributaries from the subcapsular veins (Fig. 1, b and d) and with few exceptions had anastomotic channels, not recognizable in the normal animal, with other veins in the vicinity. Thus there were variable, and variably large, communications from the ureteric vein to a lumbar vein (Fig. 1b), the ovarian or internal spermatic (Fig. 1c, d, and e), and the renal vein beyond the hilum of the kidney, either proximal or distal to the point of occlusion.

Since the renal end of the ureteric vein or veins was always enlarged, to the point where it equalled or exceeded the size of the ureter itself, it was obvious that this vein was conducting blood from the occluded renal vein. It probably also received renal blood by means of some of the enlarged capsular veins with which it connected, while blood was undoubtedly diverted from it by other capsular veins, notably those that connected the ureteric vein to a lumbar vein. Caudal to its last capsular connection the ureteric vein was sometimes diminished in size as compared with its cranial end (Fig. 1b), but in other cases (Fig. 1, c and e) there was no noticeable diminution. In all cases, apparently, some renal blood travelled downward along the ureter to reach the vesicular veins in the pelvis. In short, the ureteric vein regularly contributed to the collateral circulation from the kidney, and apparently bore some of the blood to the hypogastric vein; however, there were extrahilar connections of the ureteric vein with other veins about the kidney, and these connections contributed to the mass of enlarged veins (Fig. 2) present in the perirenal fat.

While the ureteric veins contributed a great deal to the collateral venous drainage from the kidney, it was the capsular veins and their connections which formed the major portion of the dilated vessels about the kidney. In every case the subcapsular or stellate veins were greatly enlarged on the side of obstruction of the renal vein, and in every case some of them pierced the capsule of the kidney to join the capsular veins in the perirenal fat; whether some of these represented actual new developments or all were simply enlargements of already existing channels is not known, but the number of visible connections between the subcapsular veins and the vessels in the renal fat was much greater on the side on which the renal vein had been obstructed than on the normal side, in each instance. No one of these veins piercing the renal capsule attained the size of the enlarged ureteric veins, but since they outnumbered these they were collectively carrying a significant portion of the blood from the kidney. They were not apparently constricted as they pierced the renal capsule.

The capsular veins not only drained the subcapsular veins, but they also communicated with each other and formed anastomotic channels between the larger veins in the neighborhood of the kidney. Their connections were unpredictable for any 1 animal, but collectively these vessels showed the pattern that would be anticipated, in that they emptied into all of the several vessels which normally drain the fat about the kidney (Fig. 1b, c, d, and e). The variations between specimens depended upon which of the channels were particularly enlarged, and upon the varying enlargement of connections between these channels. Thus the capsular veins emptied, below the kidney, into the upper portion of the ovarian or internal spermatic vein, into the ureteric vein, and into a lumbar vein; above the kidney, they emptied into the adrenal (adrenolumbar) vein; medially, they emptied into the patent segment of the renal vein. In some cases veins emerging from the renal capsule drained into a capsular vein which formed a large anastomotic channel (*4a* in Fig. 1c) connecting to the gonadal vein below and the adrenolumbar vein above, this channel paralleling the convex border of the kidney and corresponding to the venous perirenal arch described by Tuffier and Lejars as constantly present in man. Similarly, capsular veins receiving subcapsular ones formed channels which connected the renal vein to the adrenolumbar, or in some cases the proximal, occluded, segment of the renal vein with the distal or unoccluded segment; or they connected the ovarian, ureteric, and lumbar veins to each other in varying combinations.

Judging by the degree of enlargement of the veins, the general tendency was for the renal blood to return to the vena cava by the most direct routes. Thus the enlarged ureteric veins usually had large channels of communication to the ovarian veins when the flow in the latter was not obstructed, and to the first lumbar vein below the level of the kidney; as already noted, below their connections with the lumbar vein some ureteric veins were reduced in size, but others apparently carried most of their blood downward to the hypogastric. Similarly, the upper end of the gonadal vein was always enlarged, although in

Fig. 2. The renal region, following dissection, of a dog in which the right renal vein (on the left in the figure) was occluded close to the vena cava. This is the animal represented diagrammatically in Figure 1e. Enlarged capsular veins are visible both about the hilum and the convex border of the kidney. Further details of the venous drainage show more clearly in Figure 1e than here; note, however, the tortuous, dilated veins medial and inferior to the kidney, which are conducting renal blood, by way of the enlarged proximal end of the internal spermatic vein, into the vena cava. The light-colored ureter and the equally large but dark ureteric vein of the side operated upon show at the lower center of the picture.

only 2 cases was the ligature so placed that this vein conducted blood from the renal vein rather than to its unoccluded portion. In some cases the anastomosis of the ovarian vein with the uterine was enlarged (Fig. 1b), and apparently some blood was thus shunted to the hypogastric vein before reaching the vena cava; in others, however, this anastomosis was approximately normal in size and it was only the proximal end of the vein which was enlarged (Fig. 1d), thus giving evidence that the major portion of the extra blood received by this vein was returned directly to the vena cava (or, on the left side, to the unoccluded portion of the renal vein, and hence to the vena cava). The internal spermatic (testicular) vein was enlarged only at its cranial end (Fig. 1, c and e).

In consequence of the development and anastomoses of these channels in the perirenal fat, therefore, all of the larger veins in the neighborhood of the kidney participated in the return of its venous flow to the vena cava. This was true regardless of whether or not they normally have direct connections with the renal vein, a matter of some importance in man since in this species it is as a rule only the left renal vein that has any direct connections with veins other than the vena cava.

COMMENT

Because occlusion of the renal vein in the present experiments was carried out extrarenally, the results found here cannot exactly duplicate occlusion of the vein by a tumor, which may of course occur within the kidney itself. The procedure has nevertheless brought about the enlargement of channels which would be available for the venous drainage of the kidney regardless of whether the renal vein was occluded within or outside this organ.

That the veins found enlarged in these experiments are actually the channels which are available following occlusion of the renal vein in man is witnessed not only by the close similarity between the normal anatomy of the venous system about the kidney in dog and man, but also by the observations of Keen in a rare case of human survival of complete occlusion of the inferior vena cava from below the level of entrance of the renal veins to the level of entrance of the hepatic veins. Keen found the kidneys to be drained by greatly enlarged ureteric and capsular veins, the latter forming tortuous channels in the fat about the kidney and emptying into the adjacent larger veins. In Keen's case the return of renal blood to the heart was necessarily through connections of these larger veins to the plexus about the vertebral column, and hence to the azygos system and the superior vena cava, because of the occlusion of the inferior vena cava; in the present experiments the drainage was, in general, by the most direct route into the posterior (inferior) vena cava, and, therefore, through the larger veins in the neighborhood of the kidney —although, variably, the ovarian and ureteric veins were apparently conducting blood downward to the hypogastric veins. It was notable that in the present experiments, presumably because there was no obstruction of the vena cava itself, there was no enlargement of the deeper channels which were involved in Keen's case.

It seems to follow, therefore, that in occlusion of the renal vein in man by a tumor the same general venous channels that have been shown to be involved in the dog are the ones which show enlargement. Since any of the veins concerned with collateral drainage from the kidney could receive tumor cells through growth along their connections with the renal vein, it would seem logical to remove as many of these veins as possible in order that local recurrences of hypernephromas following nephrectomy might be minimized. From the anatomic standpoint, it is obvious that thorough removal of the perirenal fat with its enlarged venous plexuses should be done, as is customary. It would also seem proper likewise to remove abdominal portions of the ureter and the ureteric veins, and of the ovarian or internal spermatic veins, whether of the left or right side, and even the adrenal vein, and therefore the adrenal gland, of the affected side. The left gonadal and left adrenal veins in man, because of their entrance into the renal vein, offer an obvious pathway for invasion by an intravenous tumor reaching their mouths; the present experiments have

indicated, however, that the gonadal and adrenal veins may receive direct venous channels from the kidney, regardless of the level of occlusion of the renal vein, and regardless of whether they normally empty into the renal vein or the vena cava.

It is obvious from these experiments that any of the veins in the immediate vicinity of the kidney, whether or not they normally have direct connections with the renal vein, may present such connections upon occlusion of that vein, and therefore be liable to invasion by hypernephroma. Unless the incidence of such invasion is established as being very rare, removal of these veins as completely as possible would seem to offer the best opportunity to prevent recurrence of a hypernephroma which has not metastasized.

SUMMARY

Renal hypernephroma has a tendency to invade tributaries of the renal vein, and to spread by growth in continuity along veins. Growth of the tumor frequently results in occlusion of the renal vein, and in such cases dilated local venous channels subserving collateral venous drainage appear in the perirenal fat. The neoplasm is prone to recur locally following surgical removal of the kidney, and the assumption is herein made that these recurrences spring from tumor foci in collateral venous channels which were not excised at operation.

The present studies on the dog revealed that when chronic occlusion of the renal vein is produced, the collateral drainage that develops conducts blood from the kidney through enlarged subcapsular veins and their connections with veins (capsular veins) in the perirenal fat, and by enlarged intrahilar connections of the ureteral veins. From the subcapsular veins blood enters the veins in the perirenal fat, which in turn communicate with the several veins of that region, namely, the adrenal, ovarian or internal spermatic, lumbar, and ureteric veins. Blood leaving the kidney by way of the ureteral veins, principally through intrahilar connections, may flow downward to enter the vesicular veins, but also passes more directly into the vena cava by means of capsular veins which form anastomotic channels between the ureteric and the lumbar veins or others in the region of the kidney.

The collateral venous channels through which blood flows from the kidney of the dog following occlusion of the renal vein are obviously those which in man may harbor hypernephroma cells, and thus possess the ability to give rise to a recurrence of the tumor following removal of the kidney itself. It would seem advisable, therefore, to remove these collateral venous channels as completely as possible in surgical removal of the kidney for hypernephroma.

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THE USE OF STREPTOKINASE-STREPTODORNASE IN THE TREATMENT OF THORACIC EMPYEMA

JAMES J. FINNERTY, M.D., New York, New York

THE aims of treatment in thoracic empyemas are sterilization of the infected areas and early obliteration of the pleural dead spaces.

In the preantibiotic era the former was accomplished by humoral factors manufactured in the patient's own body as a reaction to the infection. Aspiration and drainage were the methods of obliterating the pleural dead spaces. These procedures incidentally reduced the number of bacteria and their toxic products that the body's immune forces had to neutralize or overcome.

The plan of treatment was to aspirate as long as the pus was thin until resolution occurred; or if thickening of the exudate rendered efficient aspiration impossible, closed drainage was instituted; and if this failed open drainage was performed after localization of the process occurred.

With the introduction of the sulfonamides and antibiotics, particularly penicillin, a new phase in the treatment of empyemas evolved.

The early treatment of pneumonias with antibiotics greatly reduced the incidence of postpneumonic empyemas, but it soon became apparent in the cases in which empyemas did develop that systemic therapy with antibiotics did not greatly influence the course of the process and that the older methods of aspiration and drainage were still required. Then Tillett, McCormack, and Cambier (11) and Butler and associates demonstrated that the local injection of penicillin into the empyema cavities rendered it possible to sterilize these spaces. But it likewise became apparent that obliteration of the pleural dead spaces was required to prevent reinfection or reactivation of suppressed infection, and again the necessity of aspiration and drainage became apparent. This method of treatment, namely local antibiotics plus frequent aspiration or closed or open drainage, was a satisfactory therapeutic method in that mortality was very low; but it was time consuming and frequently resulted in considerable pleural thickening or, more accurately, the deposition of thick fibrous membranes upon the pleural surfaces, with consequent diminution of pulmonary function.

In 1933, Tillett and Garner (10) observed that broth cultures of hemolytic streptococci are capable of rapidly lysing the fibrin clot of human blood. Milstone identified a specifically acting lysing factor present in human sera that was necessary for enzymatic streptococcal fibrinolysis. Christensen (4) contributed substantially to methods of partial purification and concentration of the fibrinolytic principle and, with MacLeod (4), developed the theory of the mechanism of action of this substance, streptokinase, which is as follows: There exists in normal blood a zymogen, which, through the kinetic action of streptokinase, is transformed into the complete enzyme, plasmin, which lyses the clot.

The streptococcal concentrates were found to be of low toxicity, and in clinical investigation proved to be capable of lysing clots in vivo, as in clotted hemothoraces, posttrauma or postpneumonectomy.

Sherry, Tillett, and Christensen (9), in 1948, observed that a large portion of the solid sediment of purulent exudates was composed not only of fibrin but also of desoxyribonucleoprotein, and that, furthermore, the streptococcal concentrate containing the fibrinolytic principle was capable of causing the rapid liquefaction of this substance in addition to the fibrin. This new factor, called streptodornase (streptococcal desoxyribonuclease), was identified as an enzyme, acting directly upon the desoxyribonucleoprotein abundantly

From the Departments of Medicine and Surgery, New York University College of Medicine, and the Third Medical and Surgical Divisions of Bellevue Hospital.

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present in purulent exudates and not requiring the presence of any factors from the blood for its activity. More recent work suggests that the streptodornase may actually consist of a series of proteolytic enzymes that attack the various degradation products occurring in the lysis of desoxyribonucleoprotein.

Thus we have a potent system of enzymes of low toxicity which are capable, in man, of lysing the principle solid components of purulent exudates, namely fibrin and desoxyribonucleoprotein.

The next step in the evolution of the treatment of empyema consisted in the injection of streptokinase-streptodornase[1] into empyema spaces in order to facilitate the evacuation of pleural exudates by aspiration, in conjunction with systemic and local antibiotics as indicated.

Tillett, Sherry, and Read (12) have reported a group of 21 cases of postpneumonic empyemas in which SK-SD was injected locally. In 18 of these cases the liquefaction of the exudates was followed by improvement that ranged from rapid and dramatic termination of the disease to marked immediate improvement followed by subsequent progressive defervescence. In 2 cases failure was due presumably to the fact that organization of the pleural membranes was well established before therapy was begun. (These 2 cases were first seen on the eighteenth and forty-first day of disease.) Ribet has similarly treated a group of empyemas with excellent results. He has also had some promising results in the early treatment of tuberculous effusions and empyemas.

In the experiences of Adie and Childress the streptococcal enzymes were valuable in thinning infected pleural exudates and permitting lung re-expansion and obliteration of the empyema spaces.

In addition to making the purulent exudate less viscous, the SK-SD seems to accomplish several other important objectives. The first is the breaking up of loculations, converting the empyema space into a single one and thus rendering it more available to the action of locally instilled antibiotics, as well as obviating the necessity of needle aspirations in multiple sites. Secondly, by lysis of the exudate, organisms presumably trapped in the fibrin mesh are liberated so as to be more available to the action of antibiotics. This is illustrated by the frequent finding that pleural cultures become negative in some cases on treatment with antibiotics but fever and exudation persist. Immediately after enzymatic therapy, cultures again become positive briefly, then permanently negative, and pleural exudation and fever subside. The third result of SK therapy is that the fibrin peel on the pleural surfaces is lysed, thus releasing the "trapped" unexpanded lung and enabling it to expand and obliterate the dead space. This débridement of the pleural surfaces probably also allows parenterally administered antibiotic, as well as the patient's own leucocytes and antibodies, to enter the infected area and exert their effect upon the infection.

An excellent example of this lysis of the pleural peel can be found in many of our cases in which there only could be obtained thin serous fluid at thoracentesis. After the injection of SK, the fluid became quite cloudy and contained lysed fibrin and nucleoproteins, undoubtedly released from the walls of the pocket. Rapid re-expansion then followed.

Reference was made earlier to the toxicity of these preparations. The only toxic effect noted in some patients from intrapleural injection is an elevation of temperature. This is usually an elevation of about 3 degrees but has been seen up to 5 and 6 degrees. It occurs within 12 to 24 hours after injection and subsides in 24 to 48 hours. This fever can usually be aborted or minimized by the oral administration of aminopyrine 0.6 gram every 6 hours, commencing some few hours before the injection and continuing for 24 hours thereafter. The basis for the pyrogenicity has not yet been determined. Its severity is not regularly related to the dosages of enzymes employed.

Concerning the actual details of treatment: the SK-SD is supplied in moisture-proof sterile ampules, each ampule containing approximately 100,000 units of SK and about ¼ that amount of SD. About 100,000 to 200,000 units of SK are diluted in 30 to 40 cubic centimeters of sterile saline and in-

[1]Subsequently referred to as SK-SD.

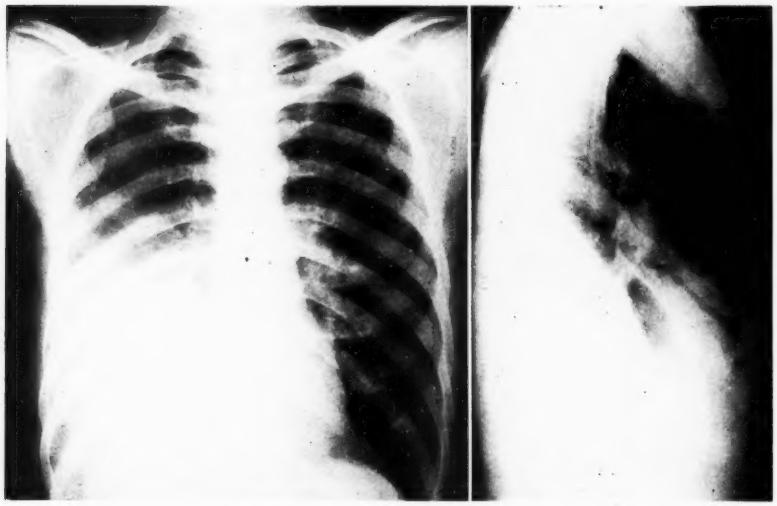

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Fig. 1.

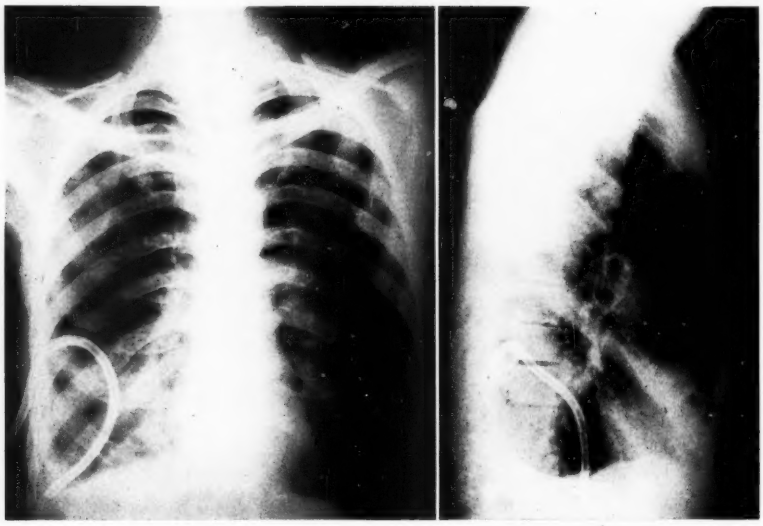

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Fig. 2.

jected into the empyema space. If the empyema is loculated, multiple smaller injections are made into several sites where fluid is obtained. From 8 to 18 hours later thoracentesis is performed. Usually, fairly large amounts of thinned exudate are easily removed, sometimes 2 to 4 liters. The chest is tapped as dry as possible and roentgenograms are then obtained. If loculations persist or if considerable opacity persists, the treatment is repeated at 48 hour intervals, or as often as deemed necessary by roentgenograms and the

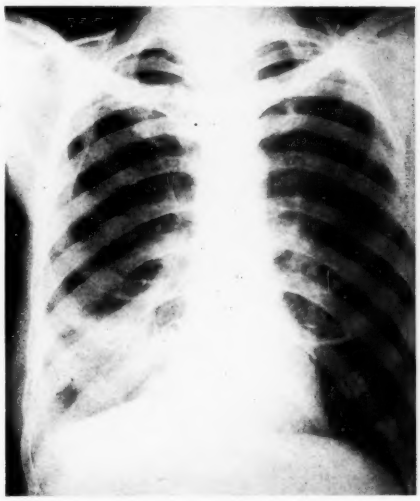

Fig. 3.

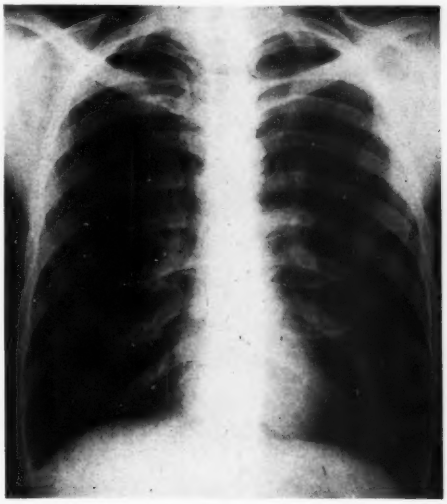

Fig. 4.

clinical course, until no more purulent exudate is obtained. The appropriate antibiotics as determined by cultures and sensitivity tests, if required, are injected along with the SK-SD.

Many patients require only one or two treatments, but some require many injections because of duration of the condition or underlying lung disease of such a nature as to keep the empyema active, for example, pulmonary suppuration, or because the amount of enzymes in a single dose do not diffuse over all the area of exudation.

This procedure has been used in several empyemas complicated by the presence of bronchopleural fistulas, presumably due to perforation of small subpleural abscesses, and in many complete resolution has occurred.

The most important practical point in therapy is that, after injection of the enzymes, aspiration, i.e., complete aspiration, must be done because the enzyme action is self-terminating and, if the lysed material is not removed, redeposition of fibrin can and will occur, and nothing will have been accomplished. The other obviously important point is that the material must be injected into the diseased area in which fluid is present; i.e., enzyme and substrate must come into contact. Most of the failures that we have seen have been due to either inadequate removal of the liquefied material or failure to inject the enzymes into the proper area in adequate dosages.

Because of this and because of the fact that patients frequently object to multiple thoracentesis, it occurred to us that the use of antibiotics and enzymes in combination with surgical closed intercostal drainage with active suction might represent a further advance in the evolution of the therapy of empyemas. The obvious advantage of this method over that just described is that better drainage of a constant nature should shorten the course of therapy, be more comfortable for the patient, and less time consuming for the physician.

Accordingly, 15 cases were treated by this method. They include such complicated situations as putrid empyemas, lung abscess with large bronchopleural fistulas, and Friedländer's abscess with fistula and empyema. The method succeeded in all cases in obliterating the empyema spaces, as well as rendering more suitable for surgery those cases in which excisional surgery was indicated by the underlying disease.

The plan used in these cases was as follows: if the empyema space was large, closed thora-

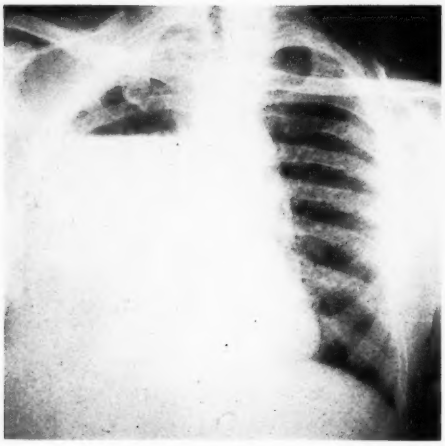

Fig. 5.

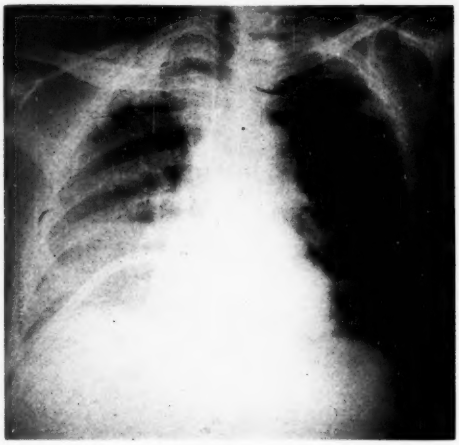

Fig. 6.

cotomy was done first under local infiltration anesthesia by using the trocar and cannula method into a dependent part of the empyema cavity. The contents were then evacuated, and enzymes instilled through the catheter, which was then clamped for 8 to 16 hours, then connected to an underwater drainage bottle to which −20 centimeters of water active suction was applied. If the pocket was small or loculated, an initial dose of SK-SD was injected, and the thoracotomy was done 8 to 16 hours later and immediately connected to underwater drainage and suction. The SK injections were made on alternate days through the tube, and the tube was clamped off for 8 to 16 hours after instillation. The tubes were removed when complete re-expansion occurred as evidenced by x-ray and clinical signs and when drainage decreased to a minimum or ceased.

Of the 15 cases treated by closed drainage and enzymes, there were 7 proved or suspected to be secondary to pneumonias and not associated with bronchopleural fistulas. The average duration of pulmonary symptoms was 20 days and varied from 7 to 42 days. Pleural cultures were positive in 4 cases.

In 6 cases, the tube was in place for an average of 3½ days, varying from 2 to 6 days, and in the seventh case it was in place for 5 weeks. This patient had the empyema for 42 days before treatment, and the long time required to obliterate the dead space illustrates the disadvantage of instituting treatment late, as organization of the pyogenic membrane had probably already begun before treatment was started.

The average number of instillations of enzymes was 2 in the early treated cases, and the average amount of drainage fluid removed by the thoracotomy tube was 2,100 cubic centimeters. The result was excellent in all of these cases.

REPORTS

CASE 1. O.T., a 49 year old white male, was admitted on February 19, 1951, with fever, cough, and malaise of 1 week's duration. The patient had had pneumonia 5 times in the last 7 years. His temperature was 101.8 degrees, pulse 116, and respirations 26. Examination of the chest revealed dullness, diminished breath sound, and crackling rales at the right base posteriorly. The patient was treated for pneumonia with terramycin for 1 week but his temperature rose to 103 degrees and roentgenogram showed a collection of fluid at the right posterior base. Aspiration on February 26, 1951, yielded 200 cubic centimeters of thick green pus. The cultures were negative. On March 2, 1951 (Fig. 1, a and b), 300,000 units of SK and 180,000 units of SD were injected intrapleurally. A closed thoracotomy was done on March 3, 1951, and 1 liter of thin green pus was removed. Roentgenogram taken immediately afterward (Fig. 2, a and b) showed remarkable clearing. The same day 300,000 units of SK and 180,000 units of SD were injected through the tube. There

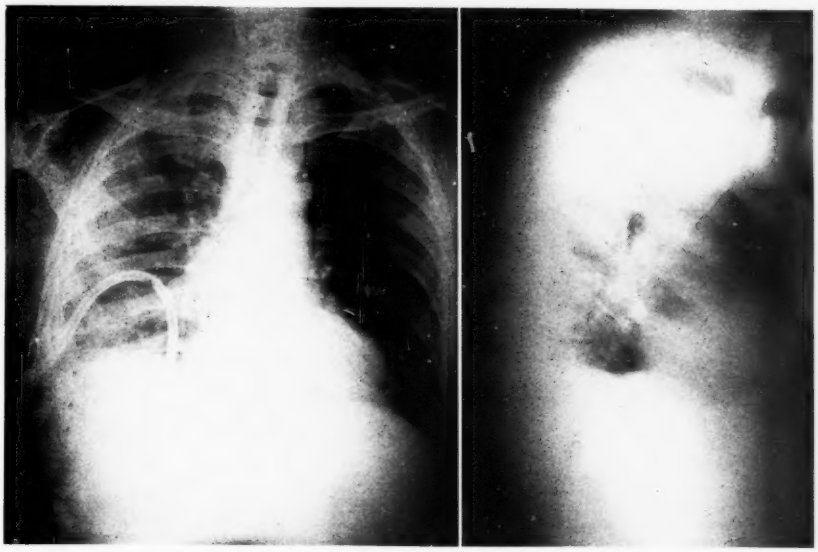

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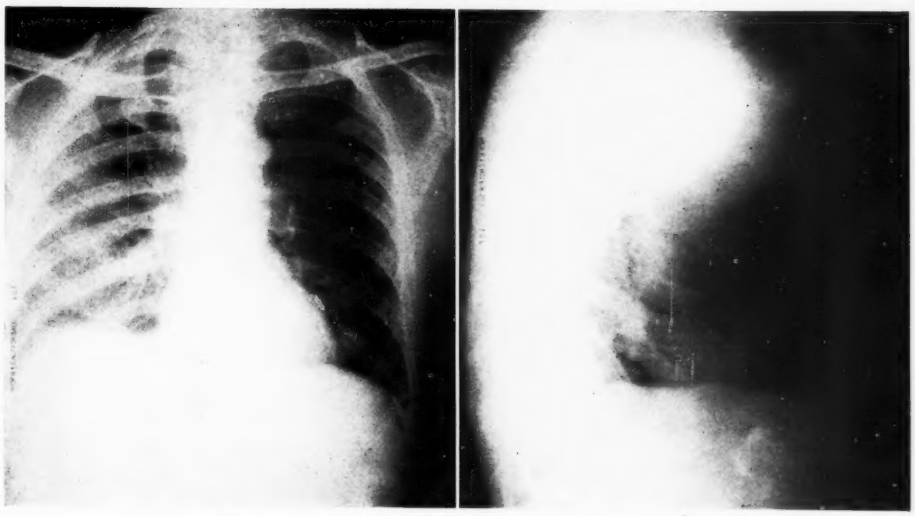
Fig. 7.



a b

Fig. 8.

was drainage of 700 cubic centimeters (Fig. 3) from the tube on March 4, 1951. On March 5, 1951 the tube was removed and the patient was afebrile. Figure 4 is a follow-up roentgenogram made on October 5, 1951.

CASE 2. H.H., a 57 year old male, was a hemiplegic from whom no history was elicited. He was admitted on April 19, 1951 with a temperature of 101.2 degrees, pulse 116, and respirations 32. Chest examination revealed dullness over the entire right

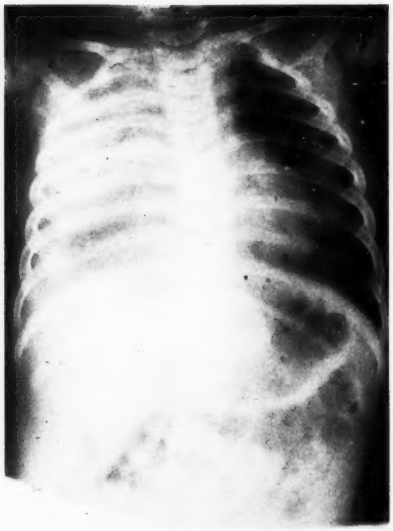


Fig. 9.

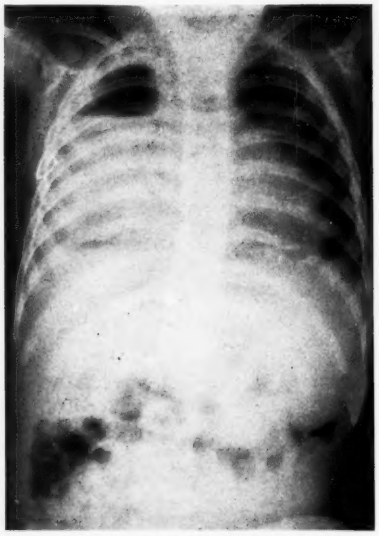


Fig. 10.

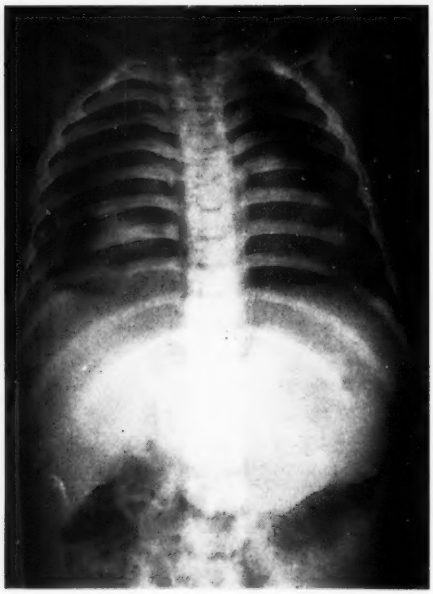


Fig. 11.

Fig. 12.

lung posteriorly with diminished breath and voice sounds. He was treated with penicillin and terramycin. A chest tap on May 9, 1951 yielded 100 cubic centimeters of thick green pus (Fig. 5, some air was accidentally admitted through needle). A culture yielded Streptococcus micros and gram negative bacteroides. On May 10, 1951 a closed thoracotomy was done. It yielded 700 cubic centimeters of pus.

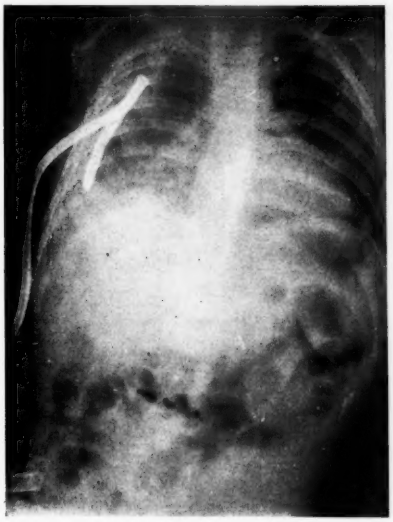


Fig. 13.

Fig. 14.

Three hundred thousand units of SK and 100,000 units of SD were injected and the tube clamped for 12 hours (Fig. 6). Another 300 cubic centimeters were drained on May 11, 1951 (Fig. 7, a and b). On May 12, 1951 300,000 units of SK and 100,000 units of SD were instilled. On May 13, 1951 there were 140 cubic centimeters of thin drainage. The tube was removed on May 16, 1951 with the temperature normal. Figure 8, a and b, was made May 17, 1951, one day after removal of the tube.

The remaining 8 cases were all associated with bronchopleural fistulas. In 6 of these cases, the fistulas closed and the empyema spaces were obliterated by closed drainage and enzyme therapy alone. The thoracotomy tube in these cases was in place for an average of 9 days and varied from 4 to 18 days. The average number of enzyme instillations was 5.

Three of these empyemas were described as foul or putrid. Although the standard treatment of this type of empyema is rib resection and open drainage plus systemic antibiotic therapy, we treated them very successfully by the closed method. Although antibiotic therapy greatly reduces the possibility of the development of a necrotizing anaerobic infection of the soft tissues of the chest wall originating at the site of closed thoracotomy, evidence of the beginning of such an infection must constantly be watched for, and if even suspected, open drainage must be promptly instituted. This was not necessary in any of our cases.

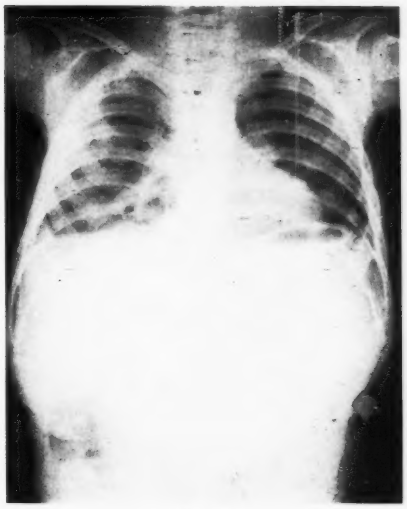
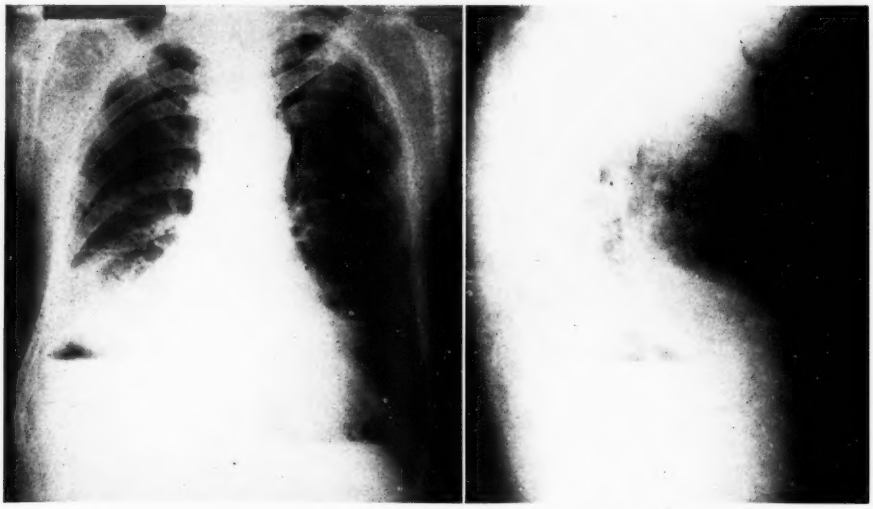


Fig. 15.

In none of the cases of fistulas did the instillation of enzymes result in expectoration of increased amounts of purulent material or



a b

Fig. 16.

a b

Fig. 17.

spread of infection to previously normal lung parenchyma, the intercostal tube apparently providing drainage adequate to prevent these sequelae.

In the 2 cases in which the fistulas persisted, there were chronic lung abscesses, requiring rib resection and drainage in 1 and lobectomy in the other. Although the preliminary treatment by closed drainage and enzymes failed to close the fistulas, and indeed we did not expect it to because of the nature of the underlying lung disease, in both pa-

Fig. 18.

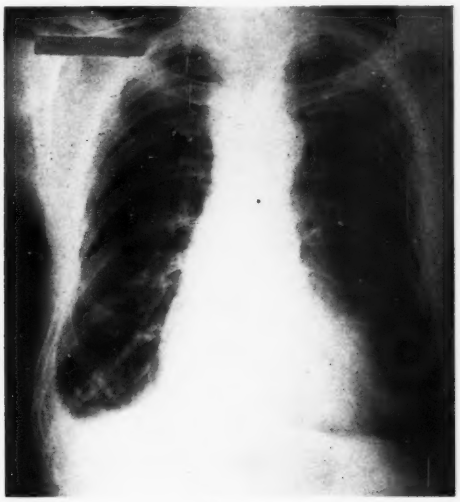


Fig. 19.

tients the sizes of the empyema spaces were greatly reduced by their therapy, and subsequent surgery was rendered easier and safer as a result.

Two of the successfully treated patients with fistulas were subsequently explored, 1 for a carcinoma of the esophagus, and 1 because of what appeared to some to be a persistent pocket. In both cases the pleural surfaces were then clean and glistening, a few filmy adhesions being the only evidence of previous infection.

CASE 3. D.R., an 11 month old female, was admitted on March 14, 1942 (Fig. 9) with right upper lobar pneumonia. Sputum cultures revealed Staphylococcus aureus sensitive to aureomycin. She was treated for 1 week with aureomycin, the fever persisted, and hydropyothorax developed (Fig. 10). Thoracentesis yielded thick creamy pus, cultures of which revealed Staphylococcus aureus. A preliminary dose of 35,000 units of SK was instilled and 8 hours later it was evident that the space had enlarged. Thoracentesis yielded 15 cubic centimeters of pus which was thinner than that previously drained (Fig. 11). On the following day (Fig. 12) closed thoracotomy was done and −5 to −20 centimeters of water suction was applied. Over the next 24 hours, no evidence of re-expansion occurred and there was very little drainage on that day. Seventy-five thousand units of SK were instilled and the tube, clamped for 8 hours, was then connected to a simple underwater seal drainage. The following morning there was almost complete re-expansion, plus about 100 cubic centimeters of thin drainage. Twenty-four hours later expansion was complete (Fig. 13), and the tube was removed 3 days later. Figure 14 was taken 2 days after removal of the tube. Figure 15 shows the situation 1 week after treatment. The temperature which was constantly elevated to 102 to 103 degrees suddenly returned to normal on the day following the second SK injection and has remained flat since.

The failure of the lung to re-expand with suction and its rapid re-expansion following an adequate dose of SK dramatically illustrate the lysis of the fibrin peel imprisoning this collapsed lung.

CASE 4. J.L., a 59 year old white male, was admitted on March 1, 1951, with a 6 weeks' history of cough which produced ½ cup of greenish, malodorous sputum. He had some fever, weight loss, and night sweats. His temperature was 101.8 degrees, pulse 84, respirations 22, and blood pressure 146/90. Chest examination revealed flatness and absent breath and voice sounds over the right base. This patient was treated with 300,000 units of penicillin every 6 hours. Thoracentesis on March 15, 1951, yielded 180 cubic centimeters of green foul pus; injected Evans' blue dye promptly appeared in the sputum (Fig. 16, a and b).

A closed thoracotomy was done on March 16, 1951. On March 18, 1951 and March 20, 1951, 300,000 units of SK were injected and a total of 1,400 cubic centimeters of drainage obtained. On March 22, 1951, (Fig. 17, a and b) the fistula was no

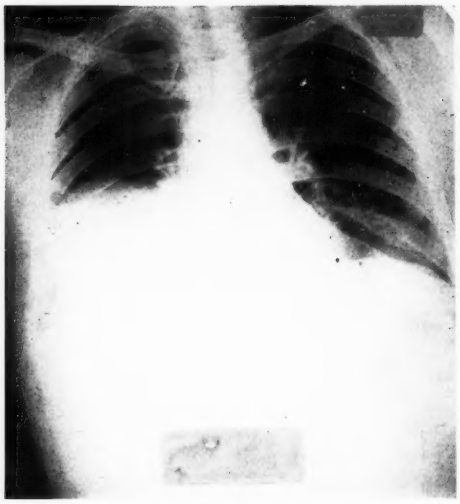


Fig. 20.

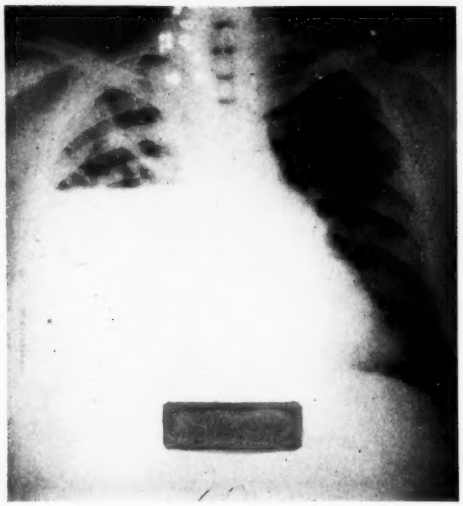


Fig. 21.

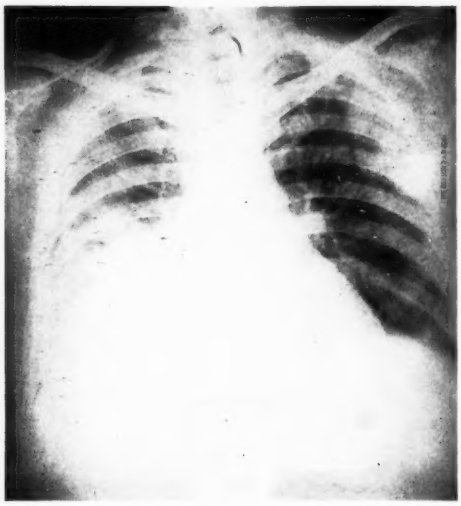


Fig. 22.

longer patent but space persisted. The patient was again treated with SK on March 23 and March 25, 1951. The tube was removed on March 27, 1951. Figure 18 taken April 3, 1951, shows good re-expansion, and a follow-up roentgenogram taken on June 4, 1951 (Fig. 19) shows further clearing.

CASE 5. P.McG., a 49 year old white male, first admitted on May 11, 1951, to the psychiatric service with toxic psychosis secondary to Friedländer pneumonia, developed an abscess of the middle lobe with empyema and bronchopleural fistula. Figure 20 is an admission film. He was treated with penicillin, streptomycin, chloromycetin, and intravenous sodium sulfadiazine. Figure 21, taken May 22, 1951, indicates that empyema and fistula were present and 300,000 units of SK were injected.

A closed thoracotomy was done on May 23, 1951. Figure 22 was made 2 days postthoracotomy. The patient was treated until May 29, 1951, when the tube was removed. Figure 23, a and b, was taken on June 19, 1951. Figure 24 was taken on August 4, 1951, immediately before the middle lobe was drained. It was found to be completely necrotic, but no residual empyema space was noted. Figure 25 taken February 1, 1952 shows the wound to be healed.

With the obliteration of the empyema space in this case, there occurred marked general improvement, with subsidence of fever and clearing of sensorium. After this, the problem was one of Friedländer's abscess uncomplicated by empyema.

We have also found SK-SD to be very useful in the preparation of unroofed empyemas for plastic closures. An example would be a case of mixed empyema unroofed by a Schede operation. Such wounds frequently resist all attempts to clean them up by the local use of antibiotics and antiseptic irrigants, such as Dakin's solution. Daily contact for several hours with the streptococcal enzymes has

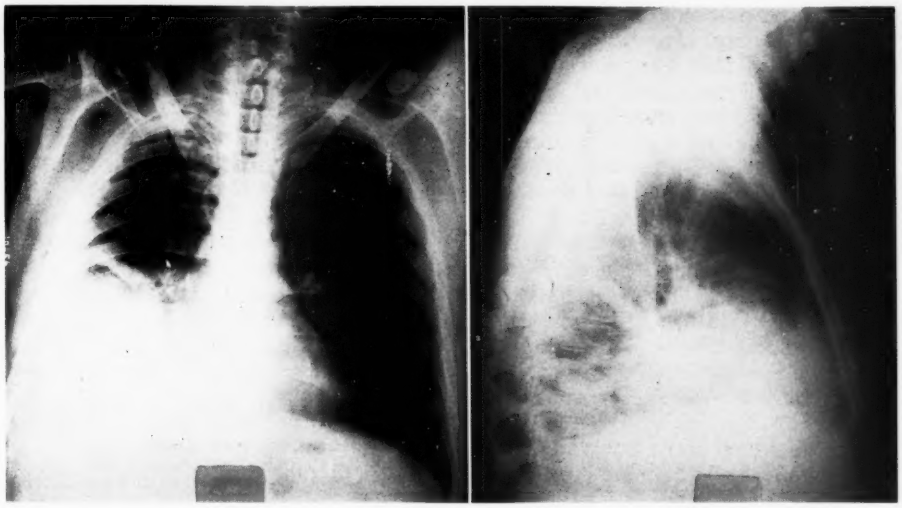


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Fig. 23.

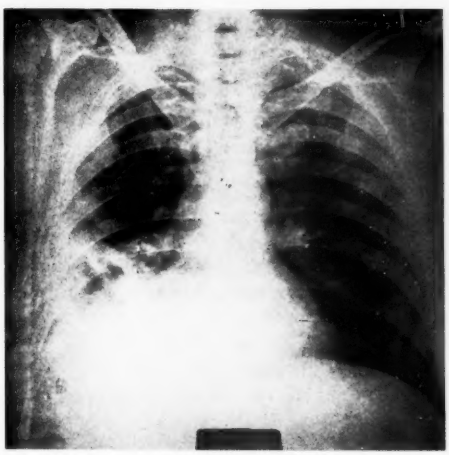

Fig. 24.

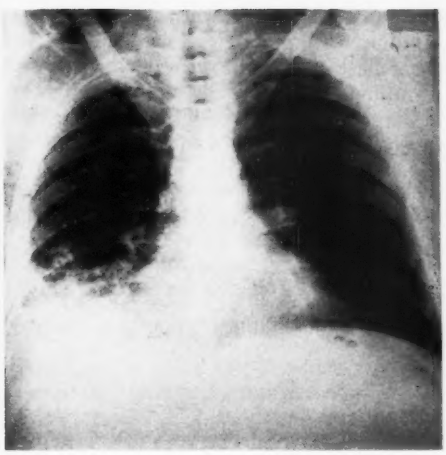

Fig. 25.

cleaned several such cavities remarkably well in short periods of time (7 to 14 days) and has produced clean, granulating wounds which were successfully closed secondarily by pectoralis and latissimus myoplasty.

CASE 6. H. M., a 47 year old white male, had previously undergone open drainage and multiple stage thoracoplasty and, finally, Schede thoracoplasty for a secondarily infected tuberculous empyema. Dirty gray exudate covered all surfaces of the pocket. After 12 days of local therapy with SK-SD, the wound was clean and granulating. Immediately thereafter the cavity was obliterated by pectoral myoplasty with delayed skin closure. An excellent result was obtained.

Recently our attention has been turned to a problem, the solution to which may prove to be one of the most important uses of SK-

SD, namely, prevention of late complications following pulmonary surgery.

It is our belief that the principal serious complications following excisional surgery of the lung, empyema, and bronchopleural fistula are the result of failure of early postoperative complete re-expansion of the remaining lobes or segments on the side operated upon. This failure of re-expansion is principally due to intrapleural clotting of blood and exudate, most of which appears to collect in the 72 hours immediately following operation. If this material is lysed by the enzymes, it can be rapidly evacuated by the intercostal catheters left in place after such operations. Suction on the catheters will then expand the lung and obliterate the space. This treatment should be instituted early, while the sutures closing the bronchial stump are intact. After 10 days to 3 weeks, these sutures may cut through, and the bronchial closure must then depend upon the fibrin coagulum until true fibrous union occurs between the cut edges of the stump. Enzymatic therapy during this intermediate period may well lyse the fibrin maintaining the bronchial closure and result in a large bronchopleural fistula. We have seen several cases in which this has occurred. Although we have not had the opportunity to treat such cases early, we know of one group of 7 cases (6) in which the results are outstanding.

SUMMARY

The streptococcal enzymes SK-SD have proved to be a valuable adjunct to the modern therapy of thoracic empyemas, and their intelligent use in conjunction with other well established therapeutic measures represents a distinct advance in the therapy of empyema.

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THE CYTOLOGIC CRITERIA OF GASTRIC CANCER

FREDERICK G. PANICO, M.D., Browning, Montana

THE cytologic smear technique continues to offer potentialities for the diagnostic identification of malignant cells found in body cavities. The application of this method to the stomach was at first discouraging because of the uncertain preservation of cells contained within the gastric aspirate. Tomenius, in a carefully controlled study of gastric material, succeeded in recognizing certain cells derived from the stomach but failed to describe malignant cells in any of the cancer cases presented in his monograph. Various early reports concerning gastric cytology were conflicting in their estimation of its general diagnostic value. Thus, poorly preserved gastric cells continued to retard gastric cytology. In 1949, the abrasive gastric balloon procedure (3) was employed as a new approach to extend cytodiagnosis to the stomach. The balloon technique succeeded in producing an increased number of well preserved gastric cells and according to Cooper and Papanicolaou has proved to be quite reliable in discovering gastric cancer.

The principle of the abrasive balloon technique is based upon the quality of abnormal gastric surface epithelial cells to cling to a rough surface. Malignant gastric cells are especially prone to exfoliate when the stomach mucosa is subjected to mechanical irritation. This observation becomes particularly significant when it is realized that normal gastric surface epithelial cells resist this type of exfoliation. Whether a deranged intercellular bridging of the individual cells undergoing atypical growth accounts for the unusual degree of friability is not certain. This cytologic alteration allows for the delivery of the gastric cells before their dissemination and disintegration within the stomach.

Material is utilized from the Cytologic Division of the Department of Anatomy, Cornell University Medical College, the Departments of Surgery of New York Hospital and Memorial Hospital for Cancer and Allied Diseases, New York, and the Departments of Surgery of the University of Maryland School of Medicine and Baltimore City Hospitals, Baltimore.

As the knowledge of the gastric cells advances through the use of the balloon technique, the practical implications for malignant diagnosis become more apparent. The amount of cellular material obtained from the stomach with the abrasive balloon appears directly proportional to the degree of gastric pathology. The large number of gastric cells retaining their cytologic detail renders adequate diagnostic material. Usually the group of malignant gastric cells (Fig. 1) will afford no problem for identification. The more profound challenge involves the recognition of the single malignant gastric cell (Fig. 2) which on the basis of certain criteria is judged pathognomonic. The accurate evaluation of the individual gastric cell is the key to the successful establishment of a negative or positive cytologic diagnosis and the essence of gastric cancer detection. In this relatively unexplored field it is hoped that the interpretation of the different cellular characteristics encountered may perhaps lay a foundation for an improved understanding of the gastric mucosal cell that eventually sheds and finds a passage of excretion through the gastric pylorus. The purpose of this presentation is to acquaint the cytologist with the individual cytologic criteria of gastric malignancy.

The gastric smear picture can reflect the condition of the gastric mucosa in the case of the different pathologic entities. A working knowledge of all cells encountered in the gastric smear becomes necessary for a proper understanding of the significant points in diagnosis. In this way the gastric cells help to form the cytologic patterns of the benign and malignant stomach. Some confirmation of this is already being supported by Henning and Witte. While certain evolving atypical characteristics have been noted in chronic disease processes, material is yet limited enough to defer any conclusive evaluation at this time. The first signal of gastric cancer becomes apparent in the gastric epithelial cell that under-

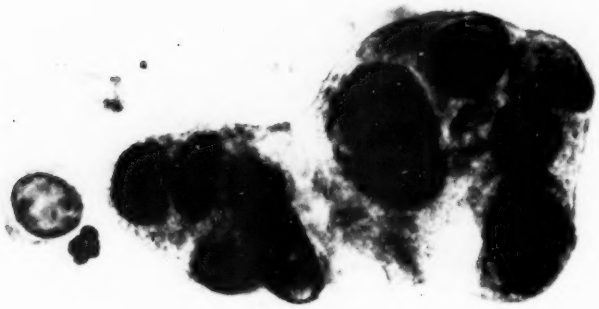


Fig. 1. Group of malignant gastric cells.

goes malignant deterioration. Therefore, the benign and malignant gastric cell will be presented for discussion.

A series of gastric cells are selected at random from over 150 stomachs to illustrate some various benign and malignant features. The identification of the gastric epithelial cell has been attained through a comparative study of all environmental cellular elements. Interpretation of the gastric cells is accomplished on the basis of associated pathologic findings. In order to establish some degree of uniformity, all cells were prepared and stained by the Papanicolaou method and all photomicrographs are reproduced at × 1160 magnification.

CELLS OF THE GASTRIC MUCOSA

The surface of the gastric mucosa consists of a simple layer of epithelial cells growing forth to line the entire gastric lumen. The smooth surface continuity of this pattern is interrupted by the many gastric pits that lead into the lumina of the gastric glands. The average nonmalignant epithelial cell from this surface layer appears in a gastric smear as a tiny cuboidal or columnar shaped basophilic cell with a small amount of polymorphous cytoplasm contained within an irregularly delineated cytoplasmic membrane (Fig. 3). The well outlined round or oval nucleus is made up of a fine and delicate staining chromatin network with a small insignificant nucleolus. The surface epithelial cells seen in a cluster formation reveal a regularity of the individual cell units with nuclei that are relatively uniform in size, shape, staining, and spacing. The secreted mucous barrier that adheres to the mucosal surface gathers many exfoliated gastric cells which shed spontaneously. Cellular remnants in the form of naked nuclei devoid of their cytoplasm are not infrequent because of the rapid cytoplasmolysis attributable to the gastric environment. These nuclear remnants may display karyorrhexis or pyknosis as a result of advancing degeneration.

The gastric glands forming the substance of the gastric mucosa are lined by a variety of gastric epithelial cell types including the mucous neck (goblet, mucous, or mucous secretory), the parietal (oxyntic, acid, or delamorphous), the chief (body chief, central, adelamorphous, or zymogenic), and the argentaffine (chromaffin) cells. All of these cells along with the surface epithelial cells are free to shed in a continuous or cyclic manner. However, the cells composing the gastric glands are first expelled into the glandular lumina where prolonged and concentrated digestion may occur before their ejection into the gastric lumen. This increased exposure to the digestive factors of the gastric secretions causes a structural alteration of the glandular epithelial cells prior to fixation. A collection of affected surface epithelial cells accessible to the abrasive balloon can be accomplished while still preserving their cytologic properties during delivery. The mucous secretory cell located at the neck of the gastric gland is occasionally

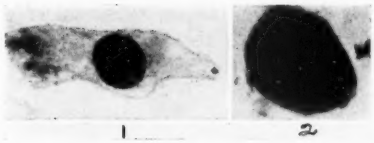


Fig. 2. Nonmalignant gastric cell (*1*); malignant gastric cell (*2*).

recognized in a smear because of a unipolar vacuolization that causes nuclear indentation. The mucoid particles collecting within the cytoplasm and compressing the nucleus may give a signet ring appearance to the mucous neck cell. These cells have to be differentiated from the nonciliated goblet cells of the naso-respiratory tract. Rarely is a parietal cell with its larger, lighter staining nucleus seen in gastric smear. Likewise, the other epithelial cells composing the deeper regions of the glandular units escape recovery because they do not come into direct contact with the balloon.

The normal histology of the gastric mucosa changes with certain disease processes. The gastric cells may reveal the evidence of such pathologic changes. Mucosal hypertrophy may be recognized because of an increased number of available surface epithelial cells interspersed with lymphocytes or polymorphonuclear leucocytes. Mucosal atrophy may be recognized when mucous neck epithelial cells appear in the relative absence of surface epithelial cells. Ulcerative lesions may be suspected when atypical epithelial cells are accompanied by inflammatory cells derived from localized mucosal reaction. These atypical cellular changes may be slight or equivocal and may often be confused with degenerative cellular changes. Malignant lesions may be discovered because certain abnormal epithelial cells demonstrate definite malignant deviations. The surface epithelial cell is seen frequently enough in gastric smear to be followed through the normal, atypical, and malignant transformations. Although in the smear picture of a diseased stomach this cell type gains primary importance in cancer diagnosis, a single atypical epithelial cell in the presence of inflammatory leucocytes should be acknowledged cautiously.

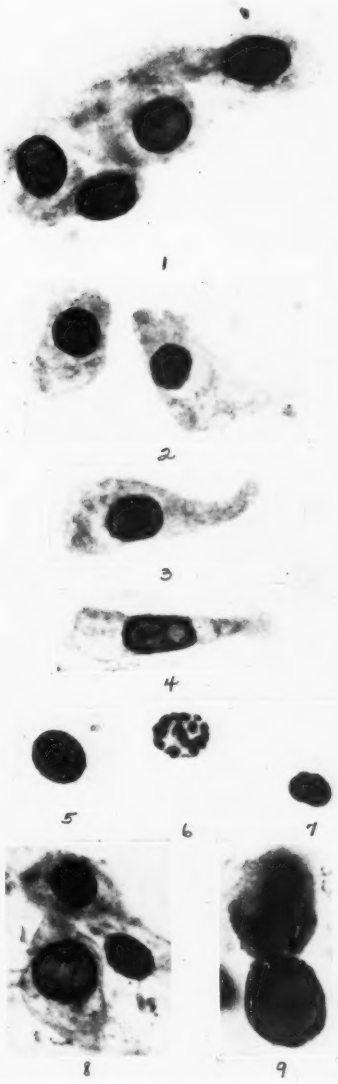


Fig. 3. Average nonmalignant surface epithelial cells from the gastric mucosa: (*1*) group of average nonmalignant surface epithelial cells; (*2*) cuboidal surface epithelial cells; (*3*) columnar surface epithelial cell with a round nucleus; (*4*) columnar surface epithelial cell with an oval nucleus; (*5*) nuclear remnant stripped of cytoplasm; (*6*) degenerating nuclear remnant showing karyorrhexis; (*7*) degenerating pyknotic nuclear remnant; (*8*) parietal gastric epithelial cell among surface epithelial cells; (*9*) mucous neck gastric epithelial cell with inclusions of mucoid particles.

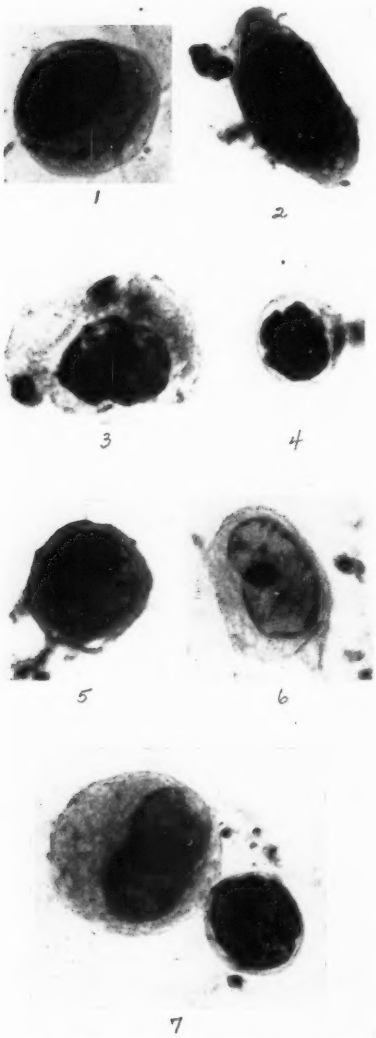


Fig. 4. The nucleus of a malignant gastric cell may feature: (*1*) enlargement; (*2*) hyperchromatism; (*3*) accessory chromatin bodies; (*4*) irregular contour; (*5*) chromatin condensation; (*6*) prominent nucleolus; (*7*) binucleation.

THE MALIGNANT GASTRIC CELL

The disorganized growth process of cancer allows the rapidly proliferating gastric cell to become available prematurely in its primordial state. Somewhat similar to the basal epithelial cell and much like a megaloblast of the erythrocytic series, the young malignant cell embodies in its structure an "activated nucleus." This nuclear activity reflects the immaturity of the cell. The recently formed tender cellular membranes reveal properties of increased pliability and permeability which probably account for many of the characteristics associated with the propagating malignant cell. The malignant gastric cell presents any combination of salient features associated with the nucleus, cytoplasm, or cell group:

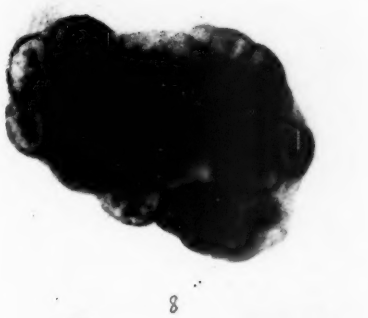
CHARACTERISTICS OF THE MALIGNANT GASTRIC CELL

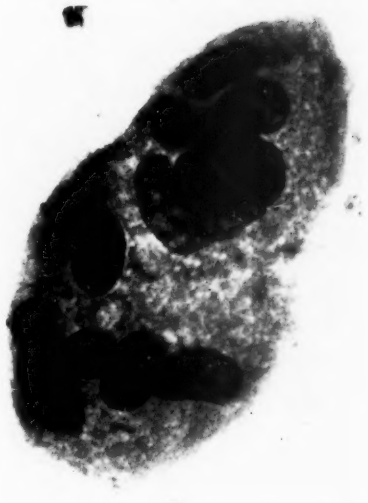
A. Nucleus may feature: (1) enlargement, (2) hyperchromatism, (3) accessory chromatin bodies, (4) irregular contour, (5) chromatin condensation, (6) prominent nucleolus, (7) binucleation, (8) multinucleation, (9) giant cell formation, (10) indentations, (11) cytoplasmic stripping, (12) ballooning, (13) fragmentation, (14) polar concentration, (15) projections, (16) vacuolar inclusions, (17) mitotic fission, and (18) gigantism.

B. Cytoplasm may feature: (1) reduced volume, (2) small vacuolar inclusions, (3) large vacuolar inclusion, (4) perinuclear vacuolization, (5) coalescence of boundaries, (6) pseudo-orangeophilia, (7) degenerating cell inclusion, (8) malignant cell inclusion, (9) polymorphonuclear leucocyte inclusion, (10) inclusions of debris, (11) lymphocytic leucocyte inclusion, and (12) irregular stringing.

C. Cell groups may feature: (1) irregular arrangement, (2) anisocytosis, (3) anisonucleosis, (4) asymmetry, (5) uneven staining, (6) superimposition, (7) crowding, and (8) pleomorphism.

The *nucleus* of the malignant gastric epithelial cell consistently shows the deteriorating change progressing within the cellular structure. A number of characteristic alterations can usually be depicted in any particular malignant nucleus (Figs. 4, 5, and 6). The enlarged nucleus gains a certain amount of hyperchromasia because accessory chromatin bodies concentrate on the inside of the nuclear shell and promote density on staining. This same membranous shell may assume any irregularity in contour. Frequently, the nucleus undergoes chromatin condensation and pyknosis. When the hyperchromasia is not intense enough to mask the detail of the chromatin network, a large nucleolus may be quite prominent among the many chromatin bodies. Binucleation is seen occasionally and may represent either a coalescence of cellular boundaries or a stage of mitosis. Multinucleation results from an exceptionally rapid proliferation of cells causing nuclear crowding





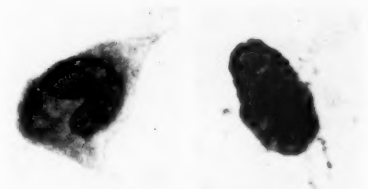
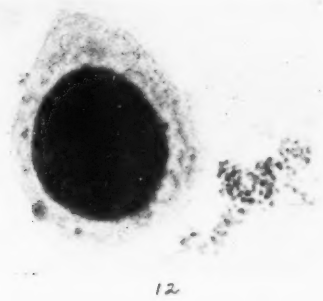
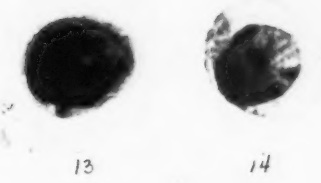


Fig. 5. The nucleus of a malignant gastric cell may feature: (*8*) multinucleation; (*9*) giant cell formation; (*10*) indentation; (*11*) cytoplasmic stripping.





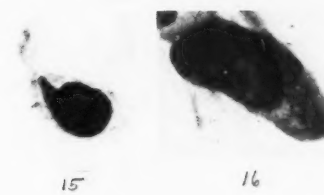


Fig. 6. The nucleus of a malignant gastric cell may feature: (*12*) ballooning with unaffected bacteria nearby; (*13*) fragmentation; (*14*) polar concentration; (*15*) projection; (*16*) vacuolar inclusions; (*17*) mitotic fission; (*18*) gigantism.

within a small area. A syncytium of abnormal cells sometimes similates a large multinucleated giant cell, in which case the nuclei are all arranged asymmetrically and lack their respective cellular boundaries. Occasionally, the nucleus becomes indented because of extrinsic compression from inclusions within the cytoplasm. Naked malignant nuclear rem-

Fig. 7. The cytoplasm of a malignant gastric cell may feature: (*1*) reduced volume; (*2*) small vacuolar inclusions; (*3*) large vacuolar inclusion; (*4*) perinuclear vacuolization; (*5*) coalescence of boundaries; (*6*) pseudo-orangeophilia with erythrocytic inclusions; (*7*) degenerating cell inclusion.

nants devoid of a cytoplasmic component appear not unlike the nucleus of an intact malignant cell. Degenerative changes are usually magnified in the nucleus that is malignant. Drying may cause the malignant cell to balloon, creating a large smudged nucleus. Increased fragility of the nucleus may be evidenced by nuclear fragmentation. The dark staining chromatin material situated on the interior surface of the nuclear membrane may cause a prominent thickening of the membrane. This same chromatin material occasionally shifts toward one pole of the membrane to effect polar concentration. Frequently the nucleus may distort into bizarre shapes. Pressure sustained during the creation of the gastric smear may be great enough to form a projection of the nucleus. Vacuolar inclusions can occur within the nucleus especially when there is a loss of the cytoplasm. While mitotic figures develop in the deeper portions of the malignant lesion, a nuclear fission is sometimes encountered. When seen, gigantism probably represents a part of the unpredictable growth activity. These are a few ways in which the malignant nucleus exhibits the unnatural process that it harbors.

The *cytoplasm* of the malignant gastric epithelial cell reveals qualities less definite than those ascribed to the nucleus (Figs. 7 and 8). The cytoplasmic volume is usually reduced in amount as the enlarged nuclear mass occupies the major part of the cell. This results in a reversed nucleocytoplasmic ratio. Multiple small or single large vacuolar inclusions may collect in the cytoplasm and even compress or encircle the nucleus. The tendency for this vacuolar formation can oftentimes be controlled by varying the concentration of the fluid media containing the cells. The cytoplasm of several cells may coalesce as their dividing boundaries disappear. Occasionally, staining reactions become significant as in pseudo-orangeophilia. Erythrocytic inclusions or extracellular hemolysis are often associated with this unusual orange color. Assimilation of heme liberated at the time of hemolysis may explain why the cytoplasm has this eosinophilic affinity. The phagocytic tendency of the immature cell is probably derived from a cytoplasmic quality associated with the young cell. As a result of this primitive characteristic, inclusions may be incorporated within the cytoplasmic mass in the

form of degenerating cells, malignant cells, polymorphonuclear or lymphocytic leucocytes, or necrotic debris. When the cytoplasmic mass is compressed during smear preparation, the effects of increased surface tension may result in fragmentation of the cytoplasmic membrane with irregular stringing. These are a few ways in which the cytoplasm of the malignant gastric cell may suggest abnormality.

The malignant *cell group* contains more than 1 cell and lends a basis for structural comparison. The cellular aggregate may not only reveal the gamut of nuclear and cytoplasmic criteria, but may present some important additional criteria (Fig. 9). The cells are assembled irregularly and present conspicuous variations in their size and shape. The cluster reveals an asymmetrical arrangement causing loss of polarity. The difference in the maturity of the individual cells may be traced through uneven staining reactions. The superimposition of the eccentrically crowded cells emphasizes the lack of restraint of the growth process. The pliable membranes of the young cells permit pleomorphism. Other architectural distortions may arise from the mechanics of smear preparation such as damage from drying (Fig. 10). This kind of degeneration might result in pyknosis or ballooning depending upon the concentration of the solution. In such ways does the cell group aid in the establishment of a positive impression.

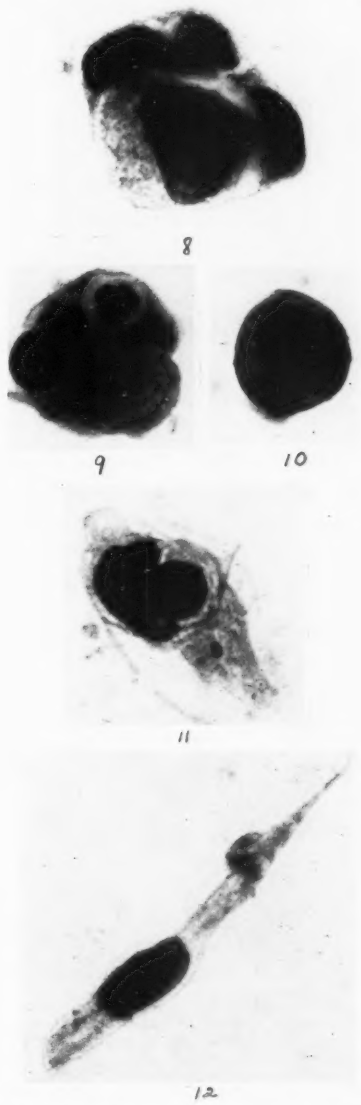


Fig. 8. The cytoplasm of a malignant gastric cell may feature: (*8*) malignant cell inclusion; (*9*) polymorphonuclear leucocyte inclusion; (*10*) inclusions of debris; (*11*) lymphocytic leucocyte inclusion; (*12*) irregular stringing.

BLOOD CELLS FROM THE GASTRIC LUMEN

Blood cells may collect in the gastric lumen with selective predominance according to the pathologic condition that is prevalent (Fig. 11). The *erythrocyte* is rarely seen in the benign gastric smear. The presence of intact, crenated, or hemolyzed erythrocytes usually suggest a malignant stomach containing a friable vascular tumor. *Polymorphonuclear leucocytes* are frequently encountered because of a reactive response to an inflammatory gastritis or to a foreign body such as a rubber tube that is introduced into the stomach. If the leucocytes are degenerating, their nuclear segments may be found fragmented or pyknotic. *Lymphocytic leucocytes* are frequently seen associated with gastritis or ulcerative processes. Size variations among the lymphocytes do occur. A general increase in their

Fig. 9. The malignant cell group may feature: irregular arrangement, anisocytosis, anisonucleosis, asymmetry, uneven staining, superimposition, crowding, and pleomorphism.

size may suggest lymphoblastic activity and may aid in the evaluation of lymphosarcoma. Unfortunately the nucleus will stain hyperchromatic and hide proper identifying features. *Plasma cells* appearing with eccentric round nuclei display a cart wheel chromatin effect which may be mistaken for degenerating polymorphonuclear leucocytes. Usually associated with large numbers of erythrocytes, their presence is suggestive of chronic inflammatory processes. *Monocytes* with slightly indented nuclei are seen occasionally in the benign stomach. *Inactive histiocytes*, although larger cells, bear a resemblance to the monocyte. The nucleus may contain a prominent nucleolus and present unipolar invagination. The inactive histiocyte is usually found discreetly isolated, a fact that helps to differentiate this type cell from the gastric surface epithelial cell. *Active histiocytes* become significant in smear because they appear when an infectious, traumatic, or tumor reaction stirs up a phagocytic response in the stomach. Presenting a variety of odd shapes, the bizarre active histiocyte is difficult to distinguish from a malignant cell. The young actively regenerating histiocytic cell reveals an enlarged hyperchromatic nucleus. Phagocytosis causes morphologic distortions of the nucleus as the cytoplasmic mass accommodates cellular inclusions by engulfment. The reparative postoperative gastric resection may also show reactive phagocytosis and yield active histiocytes with criteria that cannot be told apart from the criteria associated with true malignancy. Therefore, any active reparative process must be considered in the final interpretation of a suspected malignant stomach. This is another reason why an intelligent understanding of the gastric smear involves not only recognition of the malignant gastric cell but an integrated knowledge of the overall smear picture including the various foreign contaminating cells.

GROWTH OF GASTRIC CANCER

The balanced cycle of epithelial growth and exfoliation permits the gastric mucosal cells to regenerate at a steady rate and replace those cells that mature and eventually shed. This normal uninterrupted growth process is a function of unknown local and systemic factors. The structural activity of the surface epithelial cell remains passive depending on variables much like the bacterial colony whose morphology may be controlled by slight environmental alterations. The nidus of adenocarcinoma forms erratically along the mucosal surface of the stomach. This unicentric

or multicentric phenomenon is accompanied by characteristic abnormal cytologic trends. Whether the different epithelial cell types of the gastric mucosa are capable of producing the same malignant lesion is not clearly understood. From the gastric smear in which the surface epithelial cell is recognized with certainty, it would appear that this epithelial cell type is the cytologic unit in which adenocarcinomatous change develops. The trigger mechanism for this malignant evolution within the cell is not yet recognized.

Once initiated, the progress of gastric adenocarcinoma is divided into three different phases. The "first phase of increased exfoliation" develops as the actively proliferating atypical epithelial cells hurriedly shed from the entire free surface periphery of the lesion in an effort to accommodate newly forming cells from beneath. In this early stage, the affected epithelial cells seek the path of least resistance and exfoliate abundantly. This immature epithelial cell is undifferentiated and exhibits most of the criteria of malignancy. The increased rate of exfoliation continues effectively until the growth finds the pressure resistance equalled between the central generating focus and the surface periphery. The "second phase of local invasion" begins as the rate of cellular proliferation becomes greater than the rate of cellular exfoliation. The cells crowd themselves out of bounds and push downward into the tissues in order to cope with the lack of available space. The malignant cells forming the interior of the expanding lesion are unable to shed and find opportunity for maturing. The telltale malignant characteristics denoting the inherent quality of the abnormal epithelial cells are then temporarily masked as the cells differentiate to produce deeper papillary configurations of the invading process. The "third phase of intramural growth" is attained when the malignant epithelial cells penetrate deep enough so that proliferation becomes dependent upon the mechanics of intramural muscular activity. In this unnatural position the growth configurations will rearrange according to the muscular stresses and strains. While the malignant gastric cell is growing to adapt to its new environment, local vascular supply gradually becomes more difficult. The altered cell becomes unable to attain the substantial security of balanced nutritional demand. The metabolic equilibrium is lost and the cellular maturity is further sacrificed. Anaplastic growth develops within the muscle bundles as the malignant epithelial cells become physiologically embarrassed. In the meantime the rapidly multiplying malignant cells will still continue to exfoliate from the surface without regard to the

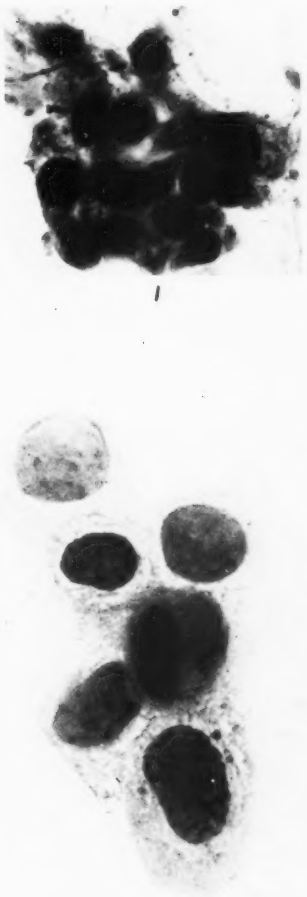


Fig. 10. Malignant cell groups may undergo architectural distortions: (*1*) pyknosis may occur as a result of drying in hypertonic medium; (*2*) ballooning may occur as a result of drying in a hypotonic medium.

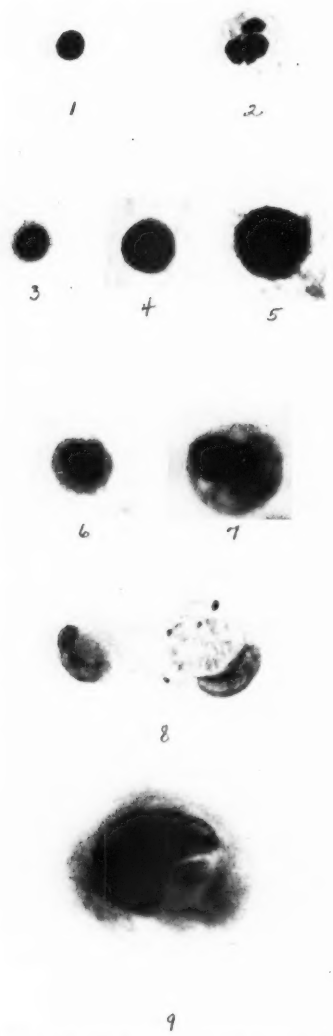


Fig. 11. Blood cells from the gastric lumen: (*1*) erythrocyte; (*2*) polymorphonuclear leucocyte; (*3*) lymphocytic leucocyte; (*4*) lymphocyte from a stomach containing lymphosarcoma; (*5*) lymphoblast from a stomach containing lymphosarcoma; (*6*) monocyte; (*7*) histiocyte (inactive form); (*8*) histiocytes (active forms) from a stomach containing reticulum cell sarcoma; (*9*) histiocyte (active form) from a stomach in a reparative stage following a subtotal gastric resection for a benign duodenal ulcer.

phase of advancing growth. Occasionally the deep seated malignant gastric cells attain surface exfoliation by the process of ulceration. When a cicatricial reaction is stimulated by the malignant growth process, a fibrotic interruption of the cancer may result if the scar replacement of the tumor occurs more rapidly than the malignant cellular propagation. This results in limitation of the invasive phase to the creeping margin of the lesion still unaffected by fibroblastic incorporation. Distant metastasis is accomplished by way of the neighboring vascular and lymphatic channels. Phagocytic activity may play a role in this tumor transference.

Presumably the surface epithelial cell is dominant in the ability to outgrow and accordingly overrun the other types of epithelial cells that would concurrently undergo atypia in the adjacent mucosa. This predominance can change. For example, the slower growing colloid type of carcinoma may be derived from some other epithelial source. With this concept of gastric cancer formation based on the deteriorating gastric surface epithelial cell, it is not difficult to understand why a pedunculated gastric polyp with early malignant change might develop a prolonged phase of increased exfoliation before local invasion occurs across the pedicle attachment; or why a small gastric ulcer surrounded with an edge of malignant epithelial cells might encourage rapid transcension of the malignant process into the phase of intramural growth. The affected cells occupy a position that promotes permeation of the deep gastric muscles by way of the penetrating ulcer base. This also explains why a lesion would have the opportunity to develop into a large bulging cellular mass if it were located at the proximal end of the stomach where there is a large potential air space, or why a lesion would result in an annular constricting mass if it were located at the distal end of the stomach where actively collapsing gastric walls are confronted with a continual pooling of injested materials. The neoplasm would receive enough trauma to cause repeated dispersion of the tumor with subsequent fibrosis.

Could it be possible that the adenocarcinomatous lesion is rare in the younger age group because there is less likelihood of acquiring a combined alteration in local and systemic fac-

tors, and more frequently established in the postmenopausal period during which time the systemic change results in atrophy associated with decreased cellular exfoliation, cellular stagnation, and increased cellular aberrations? Could this same adenocarcinomatous lesion become especially vicious in the premenopausal age when estrogenic functional peaks cause increased irritability and engender rapid intramural spread, or show slower growth advancement in the postmenopausal period when there is a decreased metabolic rate with diminished muscular activity? These are a few of the thoughts that await confirmatory proof. A good working hypothesis is oftentimes the tool that aids in constructing more concrete pathways of investigation. Cytology may yet lend the means of understanding some of the obscure malignant mechanisms developing within the stomach.

SUMMARY AND CONCLUSIONS

Gastric cytology is a growing science. Nonmalignant and malignant gastric cells are found to coexist in the same stomach. If the stomach is mechanically irritated, the malignant gastric epithelial cell will exfoliate more rapidly than the nonmalignant gastric epithelial cell. Because of this phenomenon, the malignant cell is seen frequently in the malignant gastric smear and the nonmalignant cell is seen only rarely in either the benign or malignant gastric smear.

The identity of a cluster of malignant gastric epithelial cells is not difficult. Accurate diagnosis can be made by comparing the architectural structure of the individual malignant cells seen in group arrangement. The more delicate problem involves the recognition of the single isolated malignant gastric epithelial cell which may be classified as pathognomonic on the basis of certain recognizable characteristics.

The abrasive gastric balloon has afforded the material for this study. The cellular criteria for judging the malignant from the nonmalignant gastric cell are outlined and illustrated. This presentation is offered as a basic contribution for the progressive understanding of certain fundamental features of the malignant gastric cell.

While this discussion offers only a prelude to the mysteries occurring within the diseasing stomach, the intensified study of this problem may shed light on more generalized ramifications of aberrant malignant formation. May increasing knowledge of gastric cytology be forthcoming with the availability of better preserved cells derived from the stomach.

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EDITORIALS

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AUGUST, 1953

BRING MEDICAL STUDENTS INTO VETERANS HOSPITALS—INTERCHANGE VETERANS AND CIVILIAN HOSPITAL RESIDENTS

UNDERGRADUATE teaching and resident training programs in Veterans Administration hospitals associated with medical schools are commonly conceded to be of good to excellent character and care of the patients in these hospitals to represent a signal improvement over that existing prior to World War II and the implementation of Public Law No. 293. In the Veterans Administration, speaking only of the general medical and surgical beds currently in operation, approximately 32,000 are in hospitals affiliated with medical schools or associated with Deans' Committees. However, a great number of beds, approximately 17,000, lie outside of Deans' Committee hospitals, and in these the leavening influence of teaching programs at undergraduate or resident levels is noticeably missing.

It is true that in most such hospitals varying in size from 80 to 300 beds, the Veterans Administration has provided for weekly clinical, x-ray, and pathologic conferences and that periodic visits of local and regional consultants do help as stimuli; nevertheless one must admit that the level of staff interest could be improved by the presence of bedside teaching with medical students. Hospitals of this size have neither interns, residents, nor clinical clerks and are located in small cities, often close to excellent civilian hospitals. Although occasionally in remote sections, they often lie but an hour or two distant from a medical school in need of further beds for clinical teaching.

The program recently inaugurated by Dr. Reginald Smithwick gives fourth year students at Boston University School of Medicine access to the large clinical teaching material at the Providence, Rhode Island, Veterans Hospital.

These students leave Boston on an early morning train, complete the 52 mile trip to Providence, have a morning of clinical instruction, and return in time for their afternoon classes in Boston. Members of the Providence hospital hold teaching appointments in the Boston University Faculty of Medicine. In times such as these when insurance plans have shrunken ward teaching services in civilian hospitals to a fraction of their former size and reduced their population to a preponderance of the elderly, such integrated plans are to be roundly applauded.

Logically, such participating Veterans Administration hospitals, although removed geographically from their participating medical schools, might be brought under the Deans'

Committee aegis. In this manner, although the payer of federal taxes is making a valuable contribution toward medical education, it cannot be said that "the Federal government is dictating to the medical schools."

We should now further enlarge the concept so that the surgical residents in civilian and Veterans Administration hospitals may interchange and rotate during the course of their training. Residents trained in Veterans Administration hospitals are nearly unanimous in decrying the limitations of their clinical material: the absence of children's surgery, paucity of female ailments, and of acute emergencies including traumatic conditions. One Veterans Administration surgeon, after being certified by the American Board of Surgery confessed that he had never done a radical breast operation. Others have never treated pyloric obstruction of infancy nor seen an ectopic pregnancy. Yet cases in these short categories abound in civilian hospitals offering residencies. Particularly in the fields of orthopedics, reconstructive and gastric surgery, as well as in the enlarging area of geriatrics, the Veterans Administration is rich in patients.

The majority of our residents in training today in civilian hospitals lack sufficient ward beds for their proper training. It is transparently obvious that a period of service in each type of hospital would be most beneficial to the trainees whether primarily nominated by the Veterans Administration or by the civilian institution.

It may not be amiss to remark that residents and those in residency programs should be capable of self-education. If the degree of Doctor of Medicine requires as prolonged and intensive study as the degree of Doctor of Philosophy, then resident training is actually post-postgraduate education. Perhaps some degree of spoon-feeding is permissible during intern training, but those capable of benefiting by a residency should be those capable of planning their own clinical observations, teaching, operating, rounds, and perhaps to some extent their own research.

The current philosophy of something comparable to a "40 hour week" for residents with as many nights and week-ends off duty as possible means only the degradation of opportunity. As Dunphy has said, "Time off is now regarded as compulsory as time on." The most interesting cases and the most troubling complications will continue to have a perverse way of occurring just as the whistle blows or just in the middle of the night. Continuity of observation is essential to good patient care. In fact, the very term "resident" implies living in the hospital and close to patients most of the time. As Osler "brought the student to the patient's bedside," residencies should keep him there.

But to return to our thesis and quote another example of successful integration: the University Hospitals at Iowa City now send their residents in urology and anesthesiology for definite terms to the Des Moines Veterans Administration Hospital, 120 miles distant, while the latter institution sends some of its residents to Iowa City for a part of their training. It is understood that plans are being made for the rotation of residents between the University and Veterans Administration Hospitals in Iowa City to include otolaryngology, orthopedics, surgery, and ophthalmology. Who can doubt but that such residencies become more valuable and that each of the hospitals is benefited?

The next logical step is for similar affiliations between Veterans Administration hospitals and nonuniversity hospitals of high caliber. Reinforcement of both programs can be predicted of such marriages. We can all bring to mind geographic proximities which could lend themselves to expansion of the

programs outlined. The thought must precede the deed. AUGUST F. JONAS, JR.

THE "SILENT" GALLSTONE

WHETHER or not there is such an entity as a silent gallstone is a matter of controversy. Certainly there are many physicians who feel that there is such an entity, and that in the absence of any definite symptoms referable to the biliary tract the stone should be ignored as far as surgery is concerned. Such a stone may be discovered either during a laparotomy or during a routine x-ray survey of the gastrointestinal tract. In either event, there has been no history characteristic of biliary tract disease. The number found in the manner mentioned is relatively small and many consider the stone demonstrated at the time of cholecystography, in which there are no immediate symptoms referable to the biliary tract, also to be a silent stone. This is not entirely true since the indications for taking cholecystograms are usually related to some symptoms associated with the gastrointestinal tract. It is well established that the processes which cause the formation of gallstones also cause changes in the mucosa of the gallbladder, and this leads to further alterations in the function of the gallbladder. From a strictly technical viewpoint it is more desirable to perform a cholecystectomy at the time of discovery rather than later when complications develop.

The presence of a stone or stones in a gallbladder is the precursor of several serious conditions associated with the biliary tract. Acute cholecystitis is one of these. It is rare to find such a condition without gallstones and, as has been emphasized by others, the acute attack is dependent upon previous chronic cholecystitis associated with cholelithiasis. At the onset of acute cholecystitis edema rapidly develops, not only in the wall of the gallbladder but also at the junction of the cystic and common ducts. Since this is a region of numerous anatomic variations, clear vision is of great importance in preventing injury to any of the structures of this area. A further complication which may occur in the case of acute cholecystitis is perforation. Perforation of the gallbladder during an acute episode is not frequent, but the mortality is high and the morbidity in those surviving prolonged and debilitating. Only by careful dissection can the cystic and hepatic arteries and the biliary ducts be identified and not injured. Thus the time for cholecystectomy is before an acute attack begins.

Common duct stones have been found in up to 20 per cent of cases of cholelithiasis. These stones may cause either intermittent obstruction or, when they are sufficiently large, complete obstruction. In either case there is always some damage to the liver, the degree of damage depending upon the period of complete obstruction. Often associated with common duct stones and the accompanying inflammatory reaction is either a spasm or a stenosis of the sphincter of Oddi. When this occurs even more extensive surgery is required, such as transduodenal or transcholedochal section of the sphincter. These complications can be prevented if the stone is removed before it reaches the common duct. Again cholecystectomy is indicated when the stone is found or demonstrated in the gallbladder and not after complications develop.

In most cases of carcinoma of the gallbladder, stones have been found. Some surgeons have stated that in their experience carcinoma of the gallbladder is always associated with stone. With the lengthening of the life span there seems to be an ever increasing incidence of older individuals with carcinoma of the gallbladder. One cannot help but surmise

that this is due to the long period of irritation to the mucosa of the gallbladder by the presence of stones for many years. It is most frustrating to the surgeon to operate upon a patient, suspected of having chronic cholecystitis with stones, only to find a far advanced and inoperable carcinoma involving the common or hepatic ducts. Much attention has been given to the solitary nodule of the thyroid because of the high incidence of cancer in such thyroids. By the same token it should be considered that a gallstone is an irritating factor possibly leading to carcinoma, and should, therefore, be removed at its earliest discovery.

Cardiologists have been impressed by the frequent association of coronary heart disease and gallbladder disease. The differentiation between biliary colic and an attack of angina is at times most difficult. There is a certain amount of evidence that coronary symptoms are aggravated by recurrent attacks of biliary colic. Surely it is better to remove the gallbladder early in a patient having myocardial damage than to wait until he develops one of the complications mentioned.

If the problem of cholelithiasis is considered from the standpoints mentioned, one must question the benign character of any stone. The gallstone is the main factor in the production of acute cholecystitis, common duct stones, and carcinoma of the gallbladder. A silent stone, like a silent volcano, may erupt at any time. Therefore there should be no period of watchful waiting. Cholecystectomy should be performed at the time of the discovery of the stone, and not when the complications arise. CHARLES D. BRANCH.

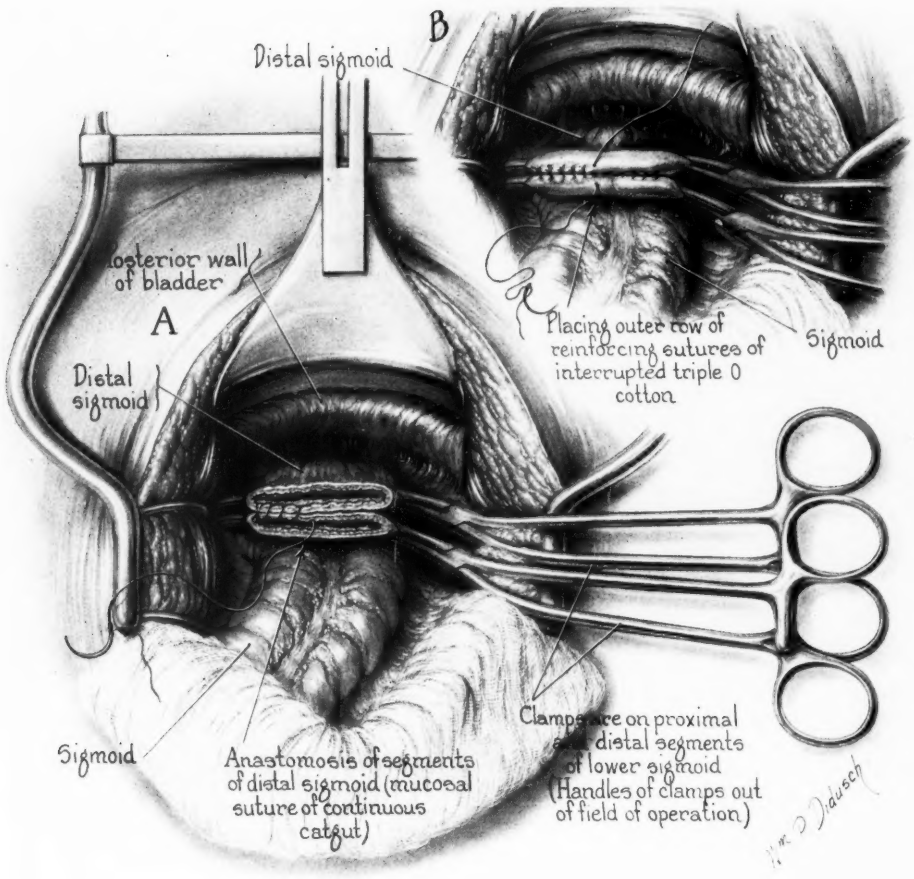
B
Distal sigmoid
Posterior wall of bladder
A
Distal sigmoid
Placing outer row of reinforcing sutures of interrupted triple 0 cotton
Sigmoid
Clamps on proximal and distal segments of lower sigmoid (Handles of clamps out of field of operation)
Sigmoid
Anastomosis of segments of distal sigmoid (mucosal suture of continuous catgut)

Fig. 2.

An Intestinal Holding Clamp for Deep Pelvic Anastomosis of the Colon.—Harold L. Foss.

THE SURGEON AT WORK

AN INTESTINAL HOLDING CLAMP FOR DEEP PELVIC ANASTOMOSIS OF THE COLON

HAROLD L. FOSS, M.D., F.A.C.S., Danville, Pennsylvania

CERTAIN operations, particularly resections utilized in the treatment of carcinoma of the sigmoid, ulcerative colitis, diverticulitis, endometriosis, and segmental ileocolitis, involve the making of an anastomosis, often deep in the pelvis and frequently in obese patients. Those who resort to procedures aimed at sphincter preservation in carcinoma of the rectum or rectosigmoid, particularly, may experience technical difficulties in carrying out the anastomosis. Partly because suitable clamps have not been devised for adequately holding the segments of the bowel while they are being united, deep pelvic anastomosis of the colon is often a difficult problem for any of us. Any such operation performed at, or close to, the anterior flexion of the peritoneum is usually difficult in obese patients, especially those with a deep pelvis. Many surgeons resort to no clamps whatever in carrying out the procedure, the operation being truly an open one. At times, such a procedure may well prove hazardous. I recently witnessed such an operation performed by one of our most skilled surgeons who, not anticipating that the patient had not been well prepared, was embarrassed by an overwhelming inundation of bowel contents. By and large, any of these procedures can best be performed if the segments of the bowel to be anastomosed are temporarily closed, gross contamination being thus prevented. In addition, suitable clamps will permit the bowel to be steadied by an assistant during the placement of the sutures.

Instruments for the purpose have been devised by Furniss, Bainbridge, Brunner, Rankin, Pemberton, and others. For years one of the most popular devices for the purpose has been the Thomas Smith clamp, one used by the author for many years but found too awkward, and none too well designed. A new instrument was gradually evolved, as herewith described, and has been used for years, with various modifications, until its present form. Since the instrument has proved especially satisfactory, it was believed worth while to call the attention of the surgical profession to it.

The clamp—which is made in pairs—is so constructed that it holds the bowel adequately and firmly yet without crushing. The reverse curves of the handles are so designed that they lie entirely without the abdomen and nearly horizontally upon it when the clamp is held in the hands of the assistant who keeps well out of the way of the surgeon. Once the resection has been carried out and the bowel segments grasped in the individual forceps of the pair, the anastomosis can be carried out by any one of a number of techniques and according to the preference of the surgeon. Interestingly enough, these forceps,

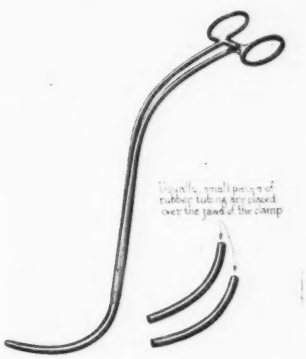

Fig. 1.

which have been used by the author in many procedures calling for rectosigmoid or sigmoid anastomosis deep in the pelvis, have proved equally satisfactory in total gastrectomies. Although originally not intended for this procedure, yet, in experiencing some difficulty in anastomosing the esophagus to the jejunum, the clamps have been resorted to and, surprisingly, found to be as helpful in this procedure as they were in the pelvis in the operations on the colon.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE 300 page monograph, *Gastric Cancer*[1] by Alfred H. Iason, is a compilation of the literature on this subject, a collective review. The subject material is divided into 13 chapters, including anatomy, histology, incidence, etiology, pathology, symptomatology, diagnosis and differential diagnosis, presurgical preparation, anesthesia, surgery, postsurgical treatment, complications, and prognosis. There is a section of references to the literature and a short index is included. While not extensive enough to serve as a complete reference work, it is at the same time too long for the average undergraduate student. There is little attempt at critical review, although some effort in this direction has been made by leaving out those things that the author considers not applicable. It is not an easy monograph to read since it so largely consists of quotations from others who have published papers on this subject, though it is true that most of the points of interest to the surgeon who is caring for gastric cancer are covered in the text. There are a number of illustrations which are quite satisfactory. The photomicrographs in general are excellent. The quality of the paper, the printing, and the binding are excellent.

THOMAS C. DOUGLASS.

THERE is an increasing trend toward large volumes in surgical textbooks. As of the present writing, *The Management of Abdominal Operations*[2] is the largest we have seen in a single book, there being 1,253 pages. Obviously, it could never be read completely, and it can be kept to serve only as a reference work. A possible minor criticism is that those most likely to benefit from the volume such as students and interns may be hesitant about including its expense in their budgets.

The general practitioner who frequently performs surgical operations will find this book helpful because of the great stress upon preoperative and postoperative treatment which, after all, is the goal indicated in the title. A very satisfactory proportion of the work deals in much detail with preoperative and postoperative care. It is interesting to note how up-to-date the references to antibiotics and other agents are, which is sometimes not the case because of the prolonged period required for collecting and editing a great number of manuscripts. There is satisfactory discussion of fluid balance. The references in this section are rather few and perhaps do not include some of the more recent contributions from American authors which have led to a standard program in most American hospitals today.

A section dealing in some detail with cancer of the esophagus and gastric cardia is most interesting, but perhaps the occasional surgeon would do better to refer such cases to the expert. As anticipated, there is a very pleasingly done section on gastric and duodenal ulcer, which we would certainly expect from Rodney Maingot. The section dealing with disease of the biliary tract is complete and stresses the proper postoperative management of various drainage tubes, a matter which the occasional operator would do well to heed diligently.

It is of interest that hernia is covered in a very short fashion, the tendency being everywhere these days to assume that the interns and residents know all about hernias. A personal quotation of Dr. J. C. Masson comes to mind: "Many of the professors would do well to leave the major resections for the residents and spend more time on the hernias."

The volume ends with a very timely chapter on aseptic surgical technique. Too often, the professors are prone to take these things for granted, hence, a few minutes devoted to demonstration of proper scrubbing, draping, and management of the operative gear are most welcome indeed.

EDWARD S. JUDD, JR.

THE authors, Dr. Conway and Dr. Stark, have created an excellent picture of the New York Hospital of one hundred years ago—the buildings, wards, private rooms, operating amphitheaters, library, the superintendents, the boards of governors, the clashes between personalities, and the struggle against the ubiquitous "surgical erysipelas" and "hospital gangrene."

In their book[3] this is the background for their portrait of Dr. Gurdon Buck, as in actuality it was the background for his work. Best remembered for his description of Buck's fascia and Buck's extension, his "other surgical innovations included excision of the knee joint and of the olecranon and successful ligation of such arteries as the common carotid, internal carotid, femoral profunda, and

[1] GASTRIC CANCER. By Alfred H. Iason. New York: Grune & Stratton, 1953.

[2] THE MANAGEMENT OF ABDOMINAL OPERATIONS. Edited by Rodney Maingot, F.R.C.S. New York: The Macmillan Co., 1953.

[3] PLASTIC SURGERY AT THE NEW YORK HOSPITAL ONE HUNDRED YEARS AGO WITH BIOGRAPHICAL NOTES ON GURDON BUCK. By Herbert Conway, M.D., and Richard B. Stark, M.D. Forewords by John Hay Whitney, Stanhope Bayne-Jones, M.D., and Frank Glenn, M.D. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1953.

common and external iliac for wounds and aneurysm. . . . . He was first in this country to approach lesions of the larynx by laryngeal fissure, . . . and his writings did much to explain the nature of acute appendicitis. Most outstanding, however, were his contributions to plastic and reparative surgery, a field in which he published twenty-one articles and a book " (*Contributions to Reparative Surgery*).

Dr. Buck's interest in reconstructive surgery was stimulated by his work on Civil War soldiers with facial wounds who were sent to the New York Hospital to be under his care. Oddly enough, the first patient was a man who had lost much of his cheek and maxilla from mercurial necrosis, a circumstance which caused the Surgeon General to eliminate calomel from the supply list of the Army.

At a time when most surgery was destructive, Dr. Buck was a pioneer in reconstructive surgery in this country, and a leader of strong character. The interwoven story of Dr. Buck and his colleagues and the New York Hospital affords an excellent example that, where such men are, great institutions will grow.

This book is replete with interesting descriptions of the then current practices and operations, illustrations of the hospital and patients, anecdotes, and many other things. To recount more of them would be a poor substitute for the pleasure of firsthand reading, which this reviewer recommends.

FRANK MCDOWELL.

THE concise work of 157 pages *The Surgery of Pancreatic Neoplasms*[1] deals with most of the phases of the surgery of pancreatic neoplasms, but there are certain omissions. For example, cysts are not considered, nor is the question of total pancreatectomy dealt with. Among the 39 case reports at the end of the text, which presumably form the basis for this treatise, instances of cysts or of total pancreatectomy are not listed, and thus these subjects quite understandably have been omitted. The work is clearly written and the reader is afforded much information without having to peruse nonessential or repititious writings. The presentation is done in a very scholarly manner beginning with the anatomy, physiology, historic review, and classification. Section II is entitled, "The center of the Problem. Carcinomas of the Ampulla of Vater and the Head of the Pancreas," and its context is obvious from the title. The reviewer is pleased to note the use of the term "pancreatoduodenectomy" rather than "pancreaticoduodenectomy," which latter term has crept into the American literature. An excellent discussion is presented. The third and final section is concerned with carcinoma of the body and tail of the pancreas, cyst adenoma and cyst adenocarcinoma, insulin producing tumors, sarcomas of the pancreas, and rare benign neoplasms of both the pancreas and the ampulla.

[1]THE SURGERY OF PANCREATIC NEOPLASMS. By Rodney Smith, M.S., F.R.C.S. Edinburgh & London: E. & S. Livingstone Ltd.; Baltimore: The Williams & Wilkins Co., 1953.

The paper is of high quality, the type is large and easily read, and of special excellence are the illustrations and diagrams.

The book is particularly suitable for those who would wish to obtain a rapid, authoritative review of most of the principle features of the surgery of pancreatic neoplasms. The reviewer applauds the action of the Council of the Royal College of Surgeons in awarding this treatise the Jacksonian Prize for 1951.

ALEXANDER BRUNSCHWIG.

THE looseleaf notebook type of publication *Hypersplenism and Surgery of the Spleen*[2] consists of approximately 80 pages which represent essentially the material presented in an exhibit at the American Medical Association meeting in 1951. Some new material has been added. The contents are divided into seven segments: the spleen, hypersplenism, hemolytic anemia, idiopathic thrombocytopenic purpura, splenomegaly, surgery of the spleen, portal hypertension and its therapy. A brief summary and a short bibliography are appended.

The entire presentation consists of an outline given in graphic form: first, of the anatomy and histology of the spleen, followed by brief notes on the physiology. The various types of disease producing splenomegaly are discussed with the results of splenectomy graphically shown. The technique for splenectomy is very nicely outlined and is illustrated by good photographs in color. While these photographs are beautifully done, they do not seem as effective to me as line drawings of the same technique might have been.

This graphic outline of the subject of hypersplenism and surgery of the spleen will be found of most use to the undergraduate student; however, the surgeon who only occasionally sees this type of disease and the surgical or medical house officer who is making his first clinical acquaintance with these diseases will find this outline by such authorities as Dameshek and Welch quite helpful.

THOMAS C. DOUGLASS.

THE authors of *Functional Disorders of the Foot*[3] are eminent orthopedic surgeons, internationally recognized as distinguished authorities. The book describes the authors' experience in office practice for the relief of many disabilities of the foot. Its purpose is to arouse an interest in the medical profession to the seriousness of disabling foot conditions and to give them the proper study and attention.

Although the authors deal primarily with the clinical aspect of foot disorders, they do include chapters on the evolutionary development of the foot, anatomy, and physiology. They stress the importance of structural and postural stability. In a

[2]HYPERSPLENISM AND SURGERY OF THE SPLEEN. By William Dameshek, M.D., and C. Stuart Welch, M.D. New York: Grune & Stratton, Inc., 1953.

[3]FUNCTIONAL DISORDERS OF THE FOOT; DIAGNOSIS AND TREATMENT. By Frank D. Dickson, M.D., F.A.C.S., and Rex. L. Diveley, A.B., M.D., F.A.C.S. 3rd ed. Philadelphia, London, Montreal: J. B. Lippincott Co., 1953.

discussion of the foot in childhood they favor a rigid type shoe in connection with which they use inlays and the Thomas heel. In the care of the adolescent they emphasize the importance of short heel cord and show surgical correction. For flat feet they use operative procedures including subtalar bone block, the stabilization operation of Hoke and of Miller, Whites' operation for congenital flat foot, and Kidner's operation, where the flat foot is due to accessory scaphoid.

In treating adults, they believe that little can be accomplished in the way of correcting faults in form and structure, therefore treatment is directed toward relieving the symptoms. There is emphasis on the importance of proper footwear, proper supports, and exercises as well as general measures to overcome any existing systemic factors.

For the correction of hallux valgus with bursitis, the authors use a type of operation in which they remove the bursitis and exostosis. In the second type operation they follow the Keller procedure, or the Mayo operation, and resect the distal end of the first metatarsal bone. For the third type, in which there is a metatarsus varus primus, they use either the Peabody, Lapidus, or McBride procedures.

Dickson's operation for intractable plantar warts is described in this new edition. The toe and metatarsal of the affected area are removed by a triangular section.

The book indicates that the authors are aware of a system of treatment by means of pliable shoes with proper correction and corrected gait to the end that pes valgo planus and many of its sequelae can be prevented and corrected and that much of the surgery for flatfoot may become unnecessary. As an ultimate objective it may be hoped that in the future treatment of abnormal foot conditions may tend more toward the elimination of causative factors with special emphasis upon prophylaxis and curative procedures rather than upon symptomatic relief.

This popular book, in its third edition, has gone far in its primary objective to stimulate interest in the medical profession to give better care for disorders of the foot. EMIL HAUSER.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

DIE GEBURTSHILFLICHEN OPERATIONEN; IHRE AUSFUEHRUNG UND ANWENDUNG. EIN LEHRBUCH FUER STUDENTEN UND GEBRAUCHSBUCH FUER AERZTE. By Prof. Dr. Med. Heinrich Martius. 7th abridged and rev. ed. 290 pages, with 268 illustrations. DM 34. Stuttgart: Georg Thieme, 1953.

THORACIC SURGICAL MANAGEMENT. By J. R. Belcher, M.S., F.R.C.S., and I. W. B. Grant, M.B., M.R.C.P. (Edin.). Foreword by Sir Clement Price Thomas. 196 pages, with 65 illustrations. $3.50. London: Baillière, Tindall & Cox; Baltimore: The Williams & Wilkins Co., 1953.

THE EPIDEMIOLOGY OF HEALTH. A New York Academy of Medicine Book. Edited by Iago Galdston, M.D. 197 pages. $4.00. New York, Minneapolis: Health Education Council, 1953.

LOCAL ANALGESIA: ABDOMINAL SURGERY. By R. R. Macintosh, M.A., D.M., F.R.C.S.(Edin.), D.A., M.D. (hon. causa), Buenos Aires, and R. Bryce-Smith, M.A., B.M., B.Ch., D.A. Illustrated by Miss M. McLarty. 94 pages, with 88 illustrations. $5.00. Edinburgh, London: E. & S. Livingstone Ltd.; Baltimore: The Williams & Wilkins Co., 1953.

TRICHLORETHYLENE ANAESTHESIA. By Gordon Ostlere, M.A., M.B., B.Chir.(Camb.), D.A. 83 pages. $2.25. Edinburgh, London: E. & S. Livingstone Ltd.; Baltimore: The Williams & Wilkins Co., 1953.

THE PHYSICIAN IN ATOMIC DEFENSE; ATOMIC PRINCIPLES, BIOLOGIC REACTION AND ORGANIZATION FOR MEDICAL DEFENSE. By Thad P. Sears, M.D., F.A.C.P. With a foreword by James J. Waring, M.D., M.A.C.P. 308 pages, with 53 illustrations. $6.00. Chicago: The Year Book Publishers, 1953.

CONDUCTION ANESTHESIA. By George P. Pitkin, M.D., F.A.C.S., F.I.C.A. Edited by James L. Southworth, Robert A. Hingson, and Winifred M. Pitkin. 2nd ed. 1,005 pages, with 585 illustrations. $22.50. Philadelphia, London, Montreal: J. B. Lippincott Co., 1953.

DISEASES OF MUSCLE; A STUDY IN PATHOLOGY. By Raymond D. Adams, M.A., M.D., D. Denny-Brown, M.D., D.Phil., F.R.C.P., and Carl M. Pearson, M.D. 556 pages, with 347 illustrations. $16.00. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., 1953.

ANNUAL REVIEW OF MEDICINE. Edited by Windsor C. Cutting and Henry W. Newman. Vol. 4. 452 pages. $6.00. Stanford, Calif.: Annual Reviews, Inc., 1953.

SURGICAL FORUM; PROCEEDINGS OF THE FORUM SESSIONS THIRTY-EIGHTH CLINICAL CONGRESS OF THE AMERICAN COLLEGE OF SURGEONS, NEW YORK CITY, SEPTEMBER, 1952. Surgical Forum Committee: Owen H. Wangensteen, M.D., F.A.C.S., Minneapolis, Chairman, J. Garrott Allen, M.D., F.A.C.S., Chicago, Warren H. Cole, M.D., F.A.C.S., Chicago, Robert E. Gross, M.D., F.A.C.S., Boston, Carl A. Moyer, M.D., F.A.C.S., Dallas, I. S. Ravdin, M.D., F.A.C.S., Philadelphia, and H. B. Shumacker, M.D., F.A.C.S., Indianapolis. 716 pages, illustrated. $10.00. Philadelphia and London: W. B. Saunders Co., 1953.

ADRENALS IN SURGERY. By E. Hasner, K. Carlsen, I. Engdahl, N. Klaerke, H. Paaby, B. Schultze, M. Sprechler, B. Sorensen, and T. Tobiassen. 107 pages, illustrated. Copenhagen: Einar Munksgaard, 1952.

THE GOLD-HEADED CANE. By William Macmichael, M.D. With a foreword by James J. Waring, M.D., and preface by William J. Kerr, M.D. New 5th ed. 187 pages, illustrated. $6.50. Springfield, Ill.: Charles C. Thomas, 1953.

THE AUTONOMIC NERVOUS SYSTEM. By Albert Kuntz, Ph.D., M.D. 4th rev. ed. 605 pages, with 94 illustrations. $10.00. Philadelphia: Lea & Febiger, 1953.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

HAROLD L. FOSS, Danville, Pennsylvania, *President*
FRED W. RANKIN, Lexington, Kentucky, *President-Elect*

PRELIMINARY PLANS FOR THE 39TH CLINICAL CONGRESS THE CONRAD HILTON HOTEL, CHICAGO OCTOBER 5 TO 9, 1953

CHICAGO's stature in the medical world continues to rise. The city has 5 accredited medical schools. Four eminent medical centers are making distinct contributions toward the progress of the health of the city and the nation: on the south side, centering around the University of Chicago, and also on the south side, around Michael Reese Hospital; on the west side, around the University of Illinois Professional Schools and Cook County Hospital; on the near north side, around Northwestern University. All these centers are now engaged in expansion programs.

Chicago is also the headquarters for many medical and related organizations. Besides the American College of Surgeons, this is the home city for the American Medical Association, the American Hospital Association, the American College of Hospital Administrators, the Joint Commission on Accreditation of Hospitals, the American Dental Association, and several prominent medical journals, among them SURGERY, GYNECOLOGY AND OBSTETRICS.

This city was the setting for the first Convocation of the American College of Surgeons which met in conjunction with the Clinical Congress of Surgeons of North America until the date of its merger with the College in 1917. In 1919 surgeons of the city and their friends presented the College with its headquarters building at 40 East Erie Street, to which was added in 1926 the John B. Murphy Memorial Auditorium.

As on previous visits, the Chicago Committee on Arrangements is making plans for a memorable Congress week, and extends a cordial welcome to visitors in the belief that this medically-minded city will be ideally suited for a successful scientific Congress.

The Congress program continues to take shape, and this issue of SURGERY, GYNECOLOGY AND OBSTETRICS will fill in further details not published in the June issue, which carried a general picture of the entire program, or in the July issue, devoted mainly to the postgraduate courses. The September number of this journal will carry the full program.

EVENING SESSIONS

There will be 3 evening sessions, to be held on Monday, Wednesday, and Friday. Tuesday and Thursday evenings will be open for special meetings.

Dr. Thomas C. Douglass, chairman of the Chicago Committee on Arrangements, will open the Presidential Meeting on Monday evening with an address of welcome. Dr. Evarts A. Graham will introduce distinguished guests, Dr. Harold L. Foss will give the Presidential Address, and Sir James Paterson Ross, London, England, will give the Eighth Martin Memorial Lecture, speaking on "Science and Surgery."

Dr. Robert H. Kennedy will preside over the Wednesday evening scientific session. The program will include: "Cardiac Arrest; Etiology and Management from a Study of Over 1,300 Cases" by J. William Hinton, New York; "Metabolic and Electrolyte Abnormalities in Severely Ill Cardiac Patients and Individuals with Advanced Cancer" by Francis D. Moore, Boston; and the Oration on Trauma by William L. Estes, Jr., Bethlehem, Pennsylvania.

New Fellows will be received into the College at the Convocation on Friday evening, and Honorary Fellowships will be conferred. The new President, Fred W. Rankin, will deliver the Fellowship Address.

GENERAL SURGERY PANEL DISCUSSIONS AND CLINICOPATHOLOGY CONFERENCES

The Congress will open at 10:30 a.m. Monday, with a panel discussion on "Management of Gastric Ulcers." Moderator: Howard K. Gray, Rochester, Minnesota. Collaborators: Joseph E. Strode, Honolulu; Claude E. Welch, Boston; and W. Keith Welsh, Toronto. Dr. Harold L. Foss will preside over this meeting. The first clinicopathology conference will be held at 1:30 p.m., with Paul R. Cannon, Chicago, acting as moderator. At 3:30 a panel discussion on "Carcinoma of the Mouth" will be held, with James Barrett Brown acting as moderator. Collaborators: John B. Erich, Rochester, Minnesota; William F. MacFee, New York; and Thomas A. Watson, Saskatoon. Speakers and subjects of other general panel discussions and clinicopathology conference follow:

Tuesday, 1:30–3 p.m.

Blood Transfusions; Complications and Their Management.
Moderator: PAUL I. HOXWORTH, Cincinnati. Collaborators: J. GARROTT ALLEN, Chicago; DOUGLAS BLAIR KENDRICK, JR.; Colonel, West Point; I. S. RAVDIN, Philadelphia; CARL W. WALTER, Boston.

Tuesday 3:30–5 p.m.

Polyposis of the Colon.
Moderator: PAUL C. MORTON, New York. Collaborators: BENTLEY P. COLCOCK, Boston; ELSON B. HELWIG, Washington, D. C.; ROBERT A. SCARBOROUGH, San Francisco.

Wednesday, 1:30–3 p.m.

Clinicopathology Conference.
Moderator: WILLIAM B. WARTMAN, Chicago.

Wednesday, 3:30–5 p.m.

Surgery of the Spleen.
Moderator: LOUIS M. ROUSSELOT, New York. Collaborators: ALEXANDER BLAIN, III, Detroit; J. ENGLEBERT DUNPHY, Boston; ROBERT H. E. ELLIOTT, New York.

Thursday, 1:30–3 p.m.

Malignant Thyroid Disease.
Moderator: OLIVER COPE, Boston. Collaborators: R. LEE CLARK, JR., Houston; BROWN M. DOBYNS, Cleveland; HENRY H. SEARLS, San Francisco.

GYNECOLOGY AND OBSTETRICS PANEL DISCUSSIONS

Wednesday, 1:30–3 p.m.

The Physiological Disorders Present in the Toxemias of Pregnancy.
Moderator: ROBERT A. ROSS, Chapel Hill. Collaborators: ALLAN C. BARNES, Columbus; RUDOLPH A. BARTHOLOMEW, Atlanta; WILLIAM J. DIECKMANN, Chicago.

Wednesday, 3:30–5 p.m.

Surgical Procedures in the Treatment of Sterility.
Moderator: JOHN ROCK, Brookline. Collaborators: WESLEY T. POMMERENKE, Rochester, New York; JAMES J. SWENDSON, St. Paul.

Thursday, 1:30–3 p.m.

Management and Problems of Prolonged Labor.
Moderator: JOHN H. MOORE, Grand Forks. Collaborators: GERALD W. GUSTAFSON, Indianapolis; C. PAUL HODGKINSON, Detroit; JOHN B. MONTGOMERY, Philadelphia.

Friday, 1:30–3 p.m.

Surgical Procedures in the Treatment of Special Defects in the Pelvic Floor Supports.
Moderator: ALBERT H. ALDRIDGE, New York. Collaborators: CHRISTOPHER J. DUNCAN, Brookline; MORRIS A. GOLDBERGER, New York; ANDREW A. MARCHETTI, Washington, D. C.; THOMAS C. PEIGHTAL, New York.

Friday, 3:15–4:45 p.m.

The Treatment of Cancer of the Cervix.
Moderator: JOE V. MEIGS, Boston. Collaborators: CONRAD G. COLLINS, New Orleans; JAMES F. NOLAN, Los Angeles; FRANKLIN L. PAYNE, Philadelphia.

PANEL DISCUSSIONS ON SURGICAL SPECIALTIES

Friday afternoon will be devoted to panel discussions on 5 surgical specialties. Topics and speakers are as follows:

Neurological Surgery

1:30–3 p.m.—The Neurosurgical Treatment of Epilepsy. Moderator: A. EARL WALKER, Baltimore. Collaborators: JOHN R. GREEN, Phoenix; H. RUSSELL MEYERS, Iowa City; THEODORE R. RASMUSSEN, Chicago.

3:15–4:45 p.m.—Cerebral Vascular Surgery. Moderator: JAMES L. POPPEN, Boston. Collaborators: ELDRIDGE H. CAMPBELL, Albany; WALLACE B. HAMBY, Buffalo, CARL F. LIST, Grand Rapids; WILLIAM H. SWEET, Boston.

Orthopedic Surgery

1:30–3 p.m.—Diagnosis and Treatment of Osteogenic Sarcoma. Moderator: MURRAY M. COPELAND, Washington, D. C. Collaborators: GRANVILLE A. BENNETT, Chicago; NORMAN L. HIGINBOTHAM, New York; H. HERMAN YOUNG, Rochester, Minnesota.

3:15–4:45 p.m.—Benign Bone Lesions Sometimes Mistaken for Sarcoma. Moderator: PAUL C. COLONNA, Philadelphia. Collaborators: CARL E. BADGLEY, Ann Arbor; G. EDMUND HAGGART, Boston; MARY S. SHERMAN, New Orleans.

Plastic Surgery

1:30–3 p.m.—Management of Compound Facial Injuries. Moderator: MINOT P. FRYER, St. Louis. Collaborators: ALBERT D. DAVIS, San Francisco; W. BOWDOIN DAVIS, Baltimore; HANS MAY, Philadelphia.

3:15–4:45 p.m.—Reconstructive Surgery of the Hand. Moderator: WALTER G. GRAHAM, Santa Barbara. Collaborators: HERBERT CONWAY, New York; JOHN TENERY, Lt. Colonel, Phoenixville; FORREST YOUNG, Redlands.

Thoracic Surgery

1:30–3 p.m.—Thoracic Emergencies. Moderator: WILLIAM M. TUTTLE, Detroit. Collaborators: THOMAS H. BURFORD, St. Louis; PAUL W. SANGER, Charlotte; HOWARD E. SNYDER, Winfield.

3:15–4:45 p.m.—Postoperative Problems in Thoracic Surgery. Moderator: PAUL C. SAMSON, Oakland. Collaborators: JOHN C. JONES, Los Angeles; JOHN D. STEELE, Milwaukee; NORMAN J. WILSON, Brookline.

Urology

1:30–3 p.m. — Urological Endocrinology. Moderator: CLYDE L. DEMING, New Haven. Collaborators: WILLIAM P. HERBST, Washington, D. C.; THOMAS D. MOORE, Memphis; SAMUEL A. VEST, Charlottesville.

3:15–4:45 p.m.—Carcinoma of the Prostate; An Appraisal of the Present Day Methods of Treatment. Moderator: J. HARTWELL HARRISON, Boston. Collaborators: ROGER C. BAKER, Chicago; GRAYSON CARROLL, St. Louis; REED M. NESBIT, Ann Arbor; PARKE G. SMITH, Miami.

OPHTHALMOLOGY PANEL DISCUSSIONS

On Tuesday evening Merrill J. Reeh, Portland, Oregon, will be the moderator for a discussion on "Surgery of the Eyelids and Adnexae." His collaborators include J. Gordon Cole, New York, Charles E. Iliff, Baltimore, and Byron Smith, New York.

On Wednesday evening Samuel J. Meyer, Chicago, will be the moderator in a discussion on the "Surgical Management of Glaucoma." The collaborators include Arthur Gerard DeVoe, New York, P. Robb McDonald, Philadelphia, and Willis S. Knighton, New York.

On Thursday evening "Surgical Management of Cataracts" will be the topic of discussion. Erling W. Hansen, Minneapolis, will moderate, assisted by Frederick C. Cordes, San Francisco, John M. McLean, New York, and Albert D. Ruedemann, Detroit.

OTOLARYNGOLOGY PANEL DISCUSSIONS

"The Tonsil and Adenoid Problem" will be discussed Tuesday evening. Gordon F. Harkness, Davenport, will be the moderator, and the collaborators will include Julius H. Hess, Chicago, Frederick T. Hill, Waterville, Dean M. Lierle, Iowa City, and C. Stewart Nash, Rochester, New York.

"Reconstructive Surgery of the Ear and Nose" will be Wednesday evening's topic, with Samuel Salinger, Chicago, as moderator. Collaborators include Lawrence R. Boies, Minneapolis, Fred Z. Havens, Rochester, Minnesota, and Jerome P. Webster, New York.

"Meniere's Syndrome" will be the subject on Thursday evening, with Leighton F. Johnson, Boston, as moderator. Collaborators include Gordon D. Hoople, Syracuse, Frank D. Lathrop, Boston, and Theodore E. Walsh, St. Louis.

MOTION PICTURES

The general theme of the ciné clinic program being developed is the audio-visual presentation of a surgical subject which stresses operative technique but which is substantially supported by photographic specimens and roentgenograms, supplemented by diagrams. It is believed that motion pictures such as these would have more permanent educational value than just the photography of a single operation. In some instances a presentation may involve photography of several operations to illustrate different points in technique or varied pathologic conditions. A partial list of topics and participants follows:

Tetralogy of Fallot. ALFRED BLALOCK
Reconstruction Common Duct. I. S. RAVDIN
Gastrojejunocolic Fistula. WARREN H. COLE
Vagotomy. LESTER R. DRAGSTEDT
Carcinoma of Ovary. HERBERT E. SCHMITZ
Hernia. LEO M. ZIMMERMAN
Pancreatic Cysts. CHARLES B. PUESTOW
Endometriosis. EDWARD D. ALLEN and LOWELL PETERSON
Tendon Injuries. MICHAEL L. MASON
Thyroid. FREDERICK A. COLLER
Carcinoma of the Lung. WILLIAM E. ADAMS
Intestinal Obstruction. CHARLES G. JOHNSTON and RUDOLPH J. NOER

Telecasts in color, will this year emanate from Albert Merritt Billings Hospital. Lester R. Dragstedt is Chairman of the Television Committee. Smith, Kline, and French are the sponsors of this feature. "Unusual Lesions in Abdominal Surgery," the theme of this year's Motion Picture Symposium, will consist of a series of short films running from 4 to 15 minutes, with a commentary by the authors.

SYMPOSIA

The Symposium on Trauma will be held on Tuesday at 2 p.m. Participants and topics are: Barnes Woodhall, "Peripheral Nerve Injuries," Rufus H. Alldredge, "Amputations," George J. Curry, "Fractures of the Ankle," Alexander P. Aitken, "Rehabilitation," Howard E. Snyder, "Trauma in a Rural Area," and Col. Glen J. Collins, "Plasma Expanders." The Symposium on Cancer will meet Wednesday at 2 p.m., with the following participants and topics: Danely P. Slaughter, "Review of the Chemotherapy of Cancer"; Richard H. Sweet, "Cancer of the Esophagus"; Owen H. Wangensteen, "Second Look"; Victor F. Marshall, "Bladder Cancer"; Norman Treves, "Breast Tumors." The Symposium on Graduate Training in Surgery and the Surgical Specialties will meet Thursday from 1:30 to 3 p.m., and the Motion Picture Symposium will be held on Thursday at 8 p.m. Further details will be announced later.

POSTGRADUATE COURSES

Details of these courses appear in the July issue of SURGERY, GYNECOLOGY AND OBSTETRICS. The broad topics to be considered and chairmen are:

Preoperative and Postoperative Care. WALTER G. MADDOCK

Surgery of the Small and the Large Bowel. R. KENNEDY GILCHRIST
Cardiovascular Surgery. EGBERT H. FELL
Obstetrics and Gynecology. HERBERT E. SCHMITZ
Trauma to the Abdomen. JAMES K. STACK
Surgery of the Upper Gastrointestinal Tract. JOHN T. REYNOLDS

The importance of immediate registration for these popular courses is emphasized again, as seating space will be limited. The registration fee is $5.00 for each course. These courses will be conducted between the hours of 8:30 a.m. and 11:30 a.m.

FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

The stimulating papers offered each year by the Surgical Forum constitute one of the prime attractions of the Clinical Congress. The Forum Committee, consisting of I. S. Ravdin, Chairman, J. Garrott Allen, Warren H. Cole, Robert E. Gross, Carl A. Moyer, and Harris B. Shumacker, Jr., is planning 12 Forum sessions. The September issue will carry this program.

ADVANCE REGISTRATIONS

No registration fee will be charged Fellows of the American College of Surgeons whose dues are paid to December 31, 1952; no registration fee is required of Initiates, Junior Candidates, or Surgical Residents. Non-Fellows and Fellows whose dues are not paid will be charged a $20.00 fee. It is suggested that non-Fellows bring medical identification with them to simplify enrollment. Official registration forms may be obtained from the American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois.

HOTEL RESERVATIONS

For hotel accommodations advance reservations are advisable. Official forms may be obtained from the American College of Surgeons.

LONDON MEETING

THE College Sectional Meeting to be held in London, May 17 to 19, 1954, preceded by the meeting of the Association of Surgeons of Great Britain and Ireland in Leeds, May 13 to 15, followed by special sessions and clinics arranged by the International Society of Surgery in Paris, and clinic visits to many other European cities, is arousing tremendous interest among American surgeons.

Surgical programs are to be presented aboard ship on the way to England. The sessions in London, star-studded with English, Canadian, and American talent, will be geared to the interests of all surgical specialists. Sir Cecil Wakeley, President of the Royal College of Surgeons of England, is Honorary Chairman of the Committee on Arrangements and is to be supported by a distinguished committee which will leave no detail untended which would add to the scientific and social attractions for visiting surgeons.

The meeting will be open to all ethical physicians and surgeons. Those who are interested in attending the meeting should communicate with Dr. Paul R. Hawley, The Director, American College of Surgeons, 40 East Erie Street, Chicago 11, Illinois.